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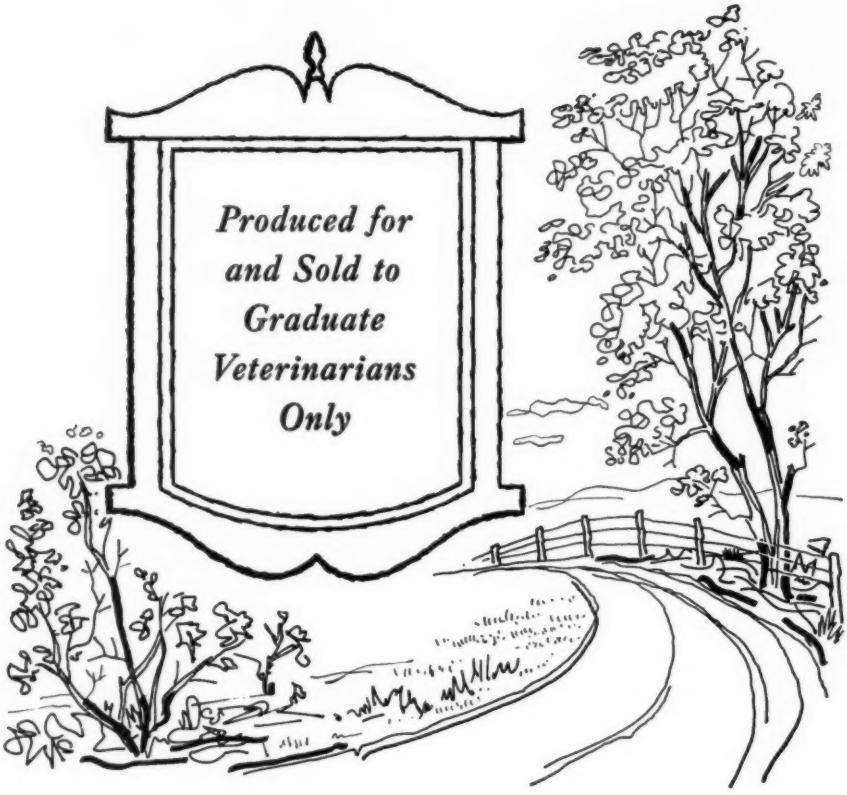

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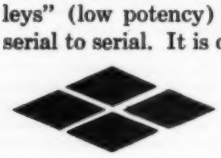

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Large Animal Practice

Where Do We Stand in Development of Professional Disease Prevention Programs?

This special VM report presents opinions and observations of 10 practitioners who have tried it.

Recently a statement was made that created quite a bit of controversy among agriculturists. This statement was, "No other industry tolerates inefficiency as does the industry of agriculture." It is true that agriculture is a business and a relatively small business compared to large businesses that exist in the United States. It's also at times a "sick business." It is going through constant changes. We are observing some tremendous changes in the business of agriculture at the present time. Many of those forecasting the future of veterinary medicine from a swivel chair within the confines of an office are not quite aware of many of the problems that exist out where livestock is raised. Fundamentally, the livestock industry is going from the small family unit to large specialized units. This shift is gradual and yet is observed throughout the entire United States.

This shift from the small inefficient operator towards a large corporate or specialized enterprise is of great concern to the veterinarian. Throughout the years, various large units in different sections of the United States have employed veterinarians either on a retainer basis or have had some type of an agreement. Fundamentally, the objective has been preventive medicine. As large units expand with specialized efforts being made toward production of livestock, the prevention of diseases becomes more important than it has ever been before. Thus, our large animal practitioners in the United States are confronted with the problem of taking a program to this phase of large animal production. The program is definitely based on preventive medicine, yet has been tagged with such names as "contract veterinary medicine," and some other terminology that has created dissension in the minds of some practitioners.

Various attempts have been presented to stimulate this type of service. Different states have had programs in their district or state meetings in which the veterinarians

discussed preventive medicine as it might be presented in an oral or written agreement. It has been termed "preventive medicine," "prearranged fee basis," "contract veterinary medicine," and "herd health programs."

Various concerns that sell drugs have developed herd health programs for the different species, outlining immunization, feeding and management practices to be sold to the livestock producer without going through the hands of the veterinarians. This has been observed from the Farm Bureau office to larger types of commercial endeavors. Thus, veterinarians are not the only ones who are concerned about this subject. There are many others who either are trying to move with the trend of times or are more concerned about the dollar than the livestock producer.

Veterinarians have expressed concern about these programs, fearing socialism, government intervention, working by contract, loss of free enterprise, ethics and many other factors that might take away freedom to practice as they desire. It is interesting to note that the majority of veterinarians who are attempting to set up preventive medicine programs have been under the ages of 35 to 40 years. It also appears that veterinarians who are working on preventive medicine are doing it in a professional manner. The majority of these veterinarians will comment that it is a new venture, that they are merely getting acquainted with the program and are trying to employ the fundamentals that were taught to them as students to prevent disease instead of merely attempting to help the sick.

Program Survey

Ten veterinarians in the Midwest who have preventive health programs were contacted and their opinions solicited on this type of veterinary practice. Seven of the 10 veterinarians indicated that they had written agreements for livestock producers and the reasons for these programs were as follows: "to promote more interest in disease prevention," "to coordinate activities of a practice on a more organized, methodical type of endeavor," "for payment of service," "to establish a closer contact with clients," "to regain some of the practice lost to lay outlets" and "to help the client raise better livestock at a greater profit."

Another veterinarian stated, "We feel it is an effective way to adequately combat the lay infringement that exists in this area. Also, it provides the farmer with a more complete veterinary service and a way to increase the financial returns for both the farmer and veterinarian." Three veterinarians indicated that the farmers requested this type of program. Seven of the 10 veterinarians thought that this type of agreement has helped their practice, while the others stated it is too early to tell.

To the question, could they see the benefits obtained from the disease prevention aspect, 5 of the veterinarians stated that the livestock owners are using practitioners more and more as consultants, both in nutrition and other management programs. One veterinarian stated that he had more than 70 farmers on a swine immunization agreement. The majority of his clients under this type of agreement get protection instead of waiting until the ravages of the various swine diseases strike their herds. He also indicated that he is vaccinating 10,000 more pigs than he did last year. Six of the veterinarians felt that they were in a position to advise the owner on management practices more than they were before.

To the question of whether they thought any aspect of this program might be criticized by the veterinary profession, the following comments were obtained. One veterinarian stated that he could understand that many practitioners might not think of these programs as being professional, and yet he was not sure of the reason, because the program was directly beneficial to the livestock producer. Another veterinarian stated the programs were not secret; anybody can examine them. Three veterinarians thought that uniform agree-

ments should be prepared by the profession for all types of livestock production so all veterinarians could benefit from them. One veterinarian stated, "It might be correct for our colleagues to charge that we are cutting prices. Since there are many practices that are dependent upon vaccination and other services are rendered at a nominal fee, we know this type of agreement with the farmer might be difficult for them to accept. Since vaccination of pigs is a procedure that definitely does not require any professional training, we do not feel that exorbitant prices are in order. Most farmers know approximately the price of biologicals at the drug store. If we continue to abuse the farmer by abnormally high charges for administration of biologicals, he will question all of our charges."

Another question which was asked covered the extent of this phase of preventive medicine. Four veterinarians indicated that they had over 50 swine producers on this type of program, while the others were just studying the program with a few. They all felt that it was as beneficial to the small producer as it was to the producer having many animals. All the veterinarians felt that if this program were not available to the livestock producer, other agencies such as feed companies and drug companies that sell directly to livestock producers would take this type of program to the livestock producer primarily with the thought of selling drugs and not services.

A few other comments obtained from the veterinarians are as follows: "I have found that this program has made good clients out of poor clients and better clients from the good clients." Another veterinarian commented that he was amazed at the pessimistic reaction of the graduating seniors from various schools of veterinary medicine in relation to the practice of veterinary medicine. He stated, "I found out that this attitude was inflicted upon them by the veterinarians who were brought in to talk to them. It is my opinion and others with whom I have talked that we are standing right on the threshold of an era in the practice of veterinary medicine that has never been equaled in quality and quantity of services or monetary returns." Four veterinarians definitely stated that they felt there was a great deal more to learn about this phase of veterinary practice, yet realized that this was fundamentally good veterinary service and had been tagged erroneously by the term "contract veterinary medicine." One veterinarian stated that if veterinary students had been taught in previous years to emphasize preventive medicine more than to attempt merely to treat the sick, lay distribution of veterinary practices and infringements that exist at the present day would have been circumvented.

Thus, throughout the United States more emphasis has been placed on preventive herd health programs and all phases of livestock production. The veterinarians who are looking over the horizon at the future of large animal practice and large animal production are taking into account the changes that are taking place in agriculture and that it is no longer strictly a way of life but a business. Thus, it must be met not only in a business way but also on a professional basis.

Management of Bovine Udder Edema

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Intense inflammation of the udder at calving time is frequently observed in the dairy breeds of cattle. There is severe edema of the mammary gland, umbilical region and escutcheon. While the incidence may be low in certain herds, Fountaine, *et al.*[1] reported that 55% of the cows in their studies were affected.

Turner[2] reported that dissection of an udder from a cow with severe edema showed mainly an excessive subcutaneous infiltration of lymph. He further reported that the skin of the udder, normally less than ¼ inch in thickness, approached 2 inches.

Swett, *et al.*[3] described the pathological findings as follows: "The swelling is limited to a layer, varying up to 2 inches in thickness, located immediately beneath the skin. It is entirely separated from the glandular tissue of the udder. The cut surface of the swollen substance appears to consist chiefly of a clear fluid containing a network of fine, silky fibers resembling a spider's web. Gross sections indicate the glandular tissues are essentially unaffected. The edema is apparently superficial and does not invade the gland proper."

Edema results in shortening of the teats, and the rigid swelling at their base makes milking very laborious (Figures 1 and 2). There is poor milk letdown. Frequently, the milk has to be discarded for long periods due to the presence of blood from ruptured capillaries.

As a result of the pendulous condition of the gland, the teats are frequently injured. The weakened edematous udder is much more susceptible to infections at this time, and subclinical bacterial infections may become established. A frequent consequence of severe edema is complete breakdown of the suspensory ligaments (Figure 3).

There is a common belief among dairymen that reducing grain feeding at this time will decrease the severity of edema. This constitutes underfeeding, inasmuch as nutrient allowances usually fall far below the levels of maintenance and production. Attention has been called to the importance of this procedure as a predisposing cause of ketosis.[4]

Following a thorough investigation, Fountaine, *et al.*[1] reported that the amount of edema at calving was not related to grain feeding during the dry period. Schmidt and Schultz[5] also found that the amount of grain fed during the dry period had no influence on edema. They concluded that udder edema is significantly correlated with milk production.

Mittelholzer[6] is of the opinion that at least 4 factors contribute to the development of excessive congestion of the udder, umbilical region and vulva.

1. The weight of the gravid uterus against the abdominal musculature interferes with the circulation of blood and lymph.

2. Increased capillary pressure associated with an increased blood volume of

pregnancy may result in escape of fluid from the vascular bed into the extravascular tissues.

3. Acceleration of physiological mammary activity during the end of pregnancy and secretion of blood proteins into colostrum may be associated with an alteration of the colloidal balance of mammary tissues.

4. A complete change in the hormone dominance of the cow at parturition influences the ion exchange of connective tissue and favors retention of sodium.

Larson and Hays[7] were the first to report the occurrence of edema and the characteristic drop in serum protein level of the blood at parturition. The drop in the serum protein level is due to the passage of globulin from the blood to the mammary gland in the process of transferring passive immunity to the newborn calf by way of the colostrum.

High producing cows tend to transfer more of these blood proteins to the colostrum, and the blood of heifers tends to reach lower levels than the cows. These observations suggested that the decrease in the blood serum protein levels at parturition, with a resultant decrease in osmotic pressure, was responsible for the edema.

Treatment

The practice of prepartum milking for the relief of udder edema is contradictory. Several investigators[8,9] have indicated that prepartum milking relieved edema, while other investigators[10,11] found the practice had little or no effect on mammary edema. Smith and Keyes[9] observed that prepartum milking relieved udder congestion in Holsteins but not in Jerseys.

Some degree of edema of the mammary system is normal in the dairy breeds. It is usually of little significance and subsides within a week following parturition. Flu-

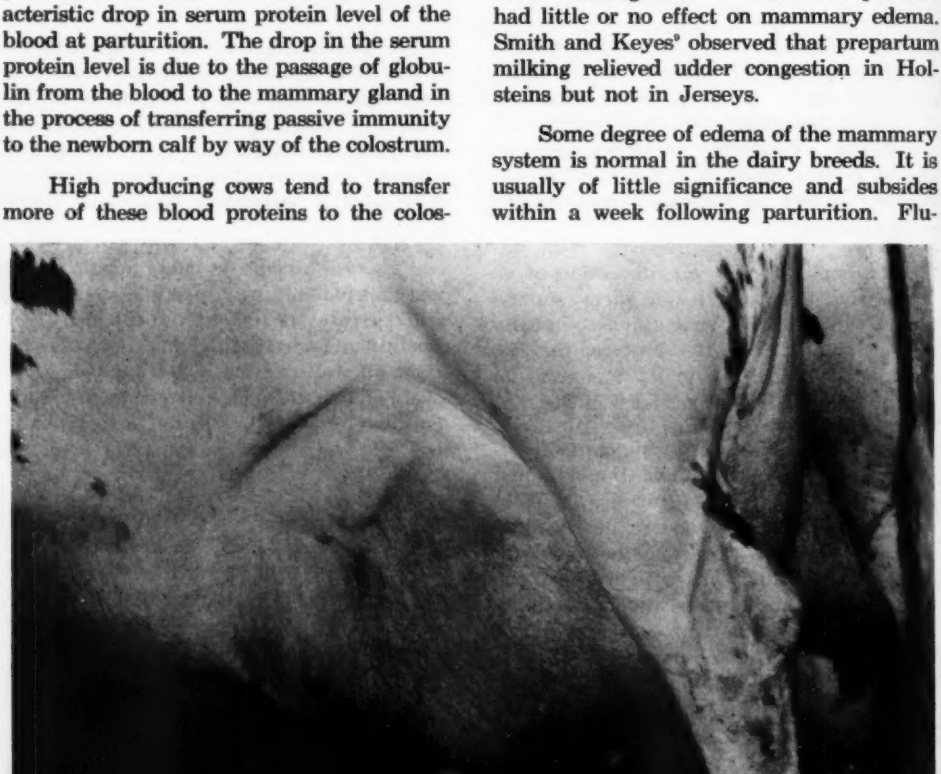

Fig. 2. Udder edema results in shortening and rigid swelling at the base of the teats, making milking very laborious.

kiger and Hofer[13] refer to this type as "physiological edema" in contrast to "chronic or pathological edema" characterized by intense inflammation and persistence. While transitory physiological edema of pregnancy rarely requires attention, severe and persistent udder edema is of considerable importance to the dairyman and warrants veterinary intervention.

Hydrochlorothiazide (Vetidrix, Ciba) is one of a new group of highly effective diuretics active by mouth.[12,14,15] In tablet form it is widely used in human medicine for the treatment of edema and hypertension. Presumably, the beneficial effects of hydrochlorothiazide in parturient edema are due to the fact that it can break one link in the chain of factors leading to edema by increasing the excretion of sodium salts. It reduces one of the osmotic factors lead- to fluid accumulation and hence causes excretion of excess water. By the temporary use of this drug, a reinstitution of the normal balance of homeostatic factors is hastened.

Structurally related to the sulfonamides, hydrochlorothiazide is a heterocyclic compound. It enhances the excretion of sodium and chloride, apparently by acting on the tubule as do the mercurials, and also inhibits carbonic anhydrase.[15] The compound causes a profound increase in the excretion of sodium and chloride in approximately equal proportions and a much smaller increase in the excretion of potassium and bicarbonate. When fluid has been retained, electrolyte excretion causes a secondary excretion of water. These actions resemble those of potent, parenterally administered mercurial diuretic agents. While mercurial preparations are toxic to cattle, hydrochlorothiazide has practically no toxicity. Daily doses of 2,500 mg. administered intramuscularly for a period of 1 week in 2 dry Ayrshire cows did not produce any apparent toxicity.

Clinical studies[8,12,16] have indicated that hydrochlorothiazide is very useful in the treatment of edematous conditions in animals. Chronic udder edema responded particularly well to an intravenous injection of 100 mg. to 150 mg. plus supplementary oral therapy repeated after 48 hours; occasionally a 3rd dose was required. Edema was generally eliminated within 4 to 7 days.

A total of 83 dairy heifers and cows from 9 herds comprising approximately 630 milking animals were employed in the investigation. Only those animals with mammary edema were selected. Although the 5 major breeds were represented, the predominating breed was Holsteins. Assignment was made at random. The same person judged the severity of edema in each herd. Hydrochlorothiazide was used as the sole therapy in this study to determine its efficacy.

Results are presented in Table 1. Generally, administration of hydrochlorothiazide was most effective when given every 48 hours. Duration of edema was reduced approximately 50% by the use of this therapy.

TABLE 1

Results Following the Use of Hydrochlorothiazide as Sole Treatment of Parturient Udder Edema in Dairy Cattle

Dosage, Route of Administration and Interval	No. of Cows	Av. Age in Months	Av. No. of Treatments	Duration of Edema Av. No. of Days
Group I 250 mg. intramuscularly every 24 hours	24	52	3	11.5
Group II 250 mg. intramuscularly every 48 hours	28	49	3	9.0
Group III Untreated Controls	31	55	0	24.0

Summary

Udder edema is mainly an excessive subcutaneous infiltration of lymph. It essentially does not involve the glandular tissue, but causes loss of milk production, predisposes the udder to injury and makes milking very laborious.

The true cause is not known. It is correlated with high milk production. The

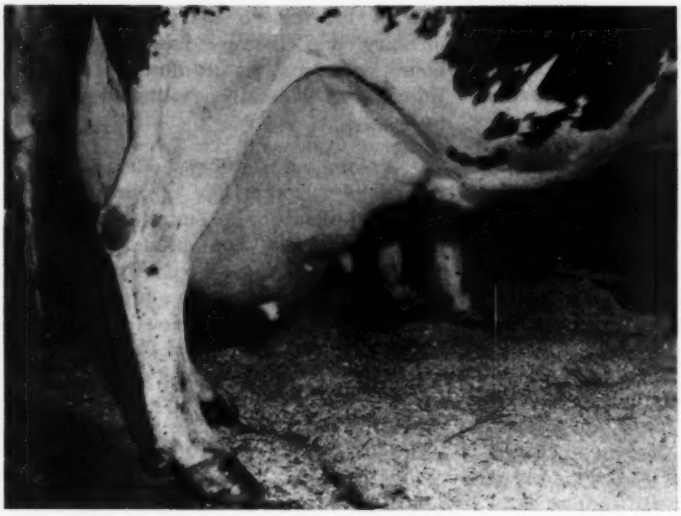

Fig. 3. Broken down suspensory ligaments is a frequent aftermath of severe udder edema.

weight of the gravid uterus, increased capillary pressure, accelerated physiological activity and change of hormone dominance at parturition are all thought to contribute. A drop in serum protein level at parturition occurs with it.

Prepartum milking is believed by some to relieve udder edema, but others do not agree. A clinical study of the use of hydrochlorothiazide is reported. Injections of 250 mg. at 48-hour intervals were found to be most effective.

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Therapeutics

Studies on Potentiation of Phenothiazine

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For 20 years, phenothiazine has been considered the most efficacious drug for the control of internal parasites of ruminants. Swanson in 1940,[1] reported that doses of 50 gm. to 80 gm. were highly effective against *Haemonchus contortus, Trichostrongylus axei, Ostertagia ostertagi,* and *Oesophagostomum radiatum* in cattle. There is good evidence that this compound is no longer effectively controlling certain internal parasites of cattle and sheep.[2,3]

Considerable work has been done with the administration of phenothiazine by different technics and in various formulas. Herlich[4] reported that there were no significant differences in the efficacy of phenothiazine administered by a capsule, bolus or water drench; however, a drench with a wetting agent appeared to be slightly more efficacious.

Douglas[5] reported that the anthelmintic efficiency of phenothiazine was inversely proportional to the diameter of the particle. Further work indicated that purified phenothiazine with a mean particle diameter of 4.8 microns was approximately equal in efficacy to that of N.F. grade with a mean particle diameter of 1.9 microns.[6]

This paper offers data on the effects of a suspension containing a combination of phenothiazine and 2-2′-dihydroxy 5-5′-dichlorodiphenylmethane (Teniatol, Pitman-Moore) on intestinal parasites. Results were based on necropsy study in sheep and on weight gains in cattle when compared with phenothiazine suspension alone.

Since the initial report on the use of 2-2′-dihydroxy 5-5′-dichlorodiphenylmethane for treating tapeworm infections in dogs,[7] the compound has been used effectively in cats, sheep, cattle, horses and humans.[8,9,10,11,12] It has also been effective in treating coccidiosis.[13,14]

Reported, uncontrolled, field tests employing a combination of equal parts of a phenothiazine suspension and 2-2′-dihydroxy 5-5′-dichlorodiphenylmethane indicated an improved anthelmintic activity over phenothiazine therapy alone.[15]

Clinical Evaluation

The suspension combining phenothiazine and Teniatol had a total drug content

of 8.5 gm. per ounce (6.25 gm. phenothiazine and 2.25 gm. Teniatol), whereas phenothiazine suspension contained 12.5 gm. of drug per ounce. Dosing with the combination was calculated on the same liquid volume as the phenothiazine suspension. For sheep under 50 lb., 1 fluid ounce; over 50 lb., 2 fluid ounces. Cattle were given 1 fluid ounce per 100 lb. body weight with a maximum of 6 fluid ounces. The suspensions were administered with a 6 ounce glass barrel dose syringe having a 9 inch length of hard rubber hose. All tests were conducted on the basis of a single drench of the anthelmintic preparations.

Statistical analysis was made of the data obtained in this critical trial (Table 1). The column headed "Analysis of Means" shows a comparison of each treatment with its control. The least significant difference (L. S. D.) was calculated at the 5% level.

Necropsy Examination: In critical studies using sheep, the animals were maintained in individual pens on concrete for 2 weeks previous to treatment. The results of 3 pre-treatment fecal examinations were used to allocate animals with similar parasite burdens to each group. Allocation was also made on body weight.

On the 7th day post-treatment all animals were sacrificed. The abomasum, small intestines and large intestines were opened and washed. The ingesta and washings were examined for parasites to be catalogued

TABLE 1
Effectiveness Based on Necropsy (critical test) in Sheep

Test Material	No. of Animals	Total Parasites Found	Mean No. of Parasites	Analysis of Means	
Trial 1 — Jan., 1960					
		Haemonchus			
None (control)	4	700	175	L.S.D.	12.27
Phenothiazine	2	200	100		4.10
Combination	4	0	0		11.15
		Trichostrongylus, Cooperia			
None (control)	4	25,700	6,425	L.S.D.	63.84
Phenothiazine	2	1,800	900		34.52
Combination	4	200	50		52.2
Trial 2 — June, 1960					
		Haemonchus			
None (control)	6	7,980	1330.0	L.S.D.	21.27
Phenothiazine	6	266	44.3		25.74
Combination	6	133	22.2		26.54
		Trichostrongylus			
None (control)	6	2,793	465.5	L.S.D.	20.18
Phenothiazine	6	1,197	199.5		4.19
Combination	6	665	110.8		7.69
		Cooperia, Nematodirus, Trichuris			
None (control)	6	7,448	1241.3	L.S.D.	23.95
Phenothiazine	6	2,394	399.0		16.45
Combination	6	2,394	399.0		15.44
		Strongyloides			
None (control)	6	665	110.8	L.S.D.	10.77
Phenothiazine	6	133	22.2		2.38
Combination	6	266	44.3		1.58

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and identified. The results of 2 trials are shown in Table 1.

Weight Gain Test: A comparison was made of weight gains of ewes and lambs following a single dose of phenothiazine and the combination. A flock of 72 ewes and 24 lambs from the same farm was individually weighed, ear tagged and dosed on June 2, 1960. Three weeks later all animals were re-weighed. Table 2 shows the difference in weight gains of ewes and lambs following a single treatment with phenothiazine or the combination.

A group of 247 yearling feeder calves was used to determine the efficacy of the combination in comparison with nontreated controls and to those treated with phenothiazine alone. Calves were run through a cutting corral, weighed, ear tagged and dosed with the allocated medicant on June 30, 1960. All animals were re-weighed 5 weeks later. The weight gains of the cattle following treatment are shown in Table 3.

Discussion

The decision on frequency of dosing is often a difficult one for the veterinarian. In some herds and flocks, one treatment can bring about cessation of deaths and increased weight gains. In other groups of animals where severe reinfection exists and "immunity" develops more slowly, it may be necessary to dose 2 or 3 times at 2 to 3 week intervals, then monthly thereafter. There obviously cannot be a routine or standard dosing program set up for all groups of animals. This is especially true in the southern part of our country where clinical parasitism is such a common and severe problem. Severe internal parasitism, which has discouraged sheep production in this area, can be controlled by realistic dosing programs designed to help the animals live with the problem. Ideally, a "parasite free" animal is the ultimate goal, but in usual animal husbandry practices, the situation is not likely to occur. In veterinary practice the aim is to bring parasitic diseases under control to the point where the parasite infection produces little detrimental effect (loss of weight) in the host animal.

The effectiveness of an anthelmintic can be based on: (1) necropsy study of the parasite load following treatment, (2) pre- and post-treatment parasite ova counts, (3) incidence of death loss and (4) weight gains.

In this study the results were based on the critical necropsy test in sheep and weight gains in sheep and cattle. A preliminary critical trial indicated that the combination was equal or superior to an equal volume of phenothiazine suspension in removing *Haemonchus* sp., *Trichostrongylus* sp. and *Cooperia* sp.

The results of the 2nd critical test showed that the combination was statistically significant in removing *Haemonchus* sp. The combination approached significance at the 5% level in removing *Cooperia* sp., *Nematodirus* sp. and *Trichuris* sp. There was a close correlation of results achieved by the combination and that of phenothiazine suspension.

The sheep weight gain showed the combination was significantly better than phenothiazine alone in the ewes, but the 2 treatment programs were effective to the same degree on the lambs. The ewes receiving phenothiazine suspension gained 6.33 lb., while those receiving the combination gained 9.64 lb. The difference in gains of 3.31 lb. was significant.

The cattle weight gain test clearly demonstrated the combination was significantly more effective than phenothiazine

TABLE 2

Sheep Experiment Weight Gain Following One Dose

Animals & Material Used	Number of Animals	Treatment Means (weight gains in pounds)	Analysis of Means
Ewes			
Phenothiazine	36	6.33	L. S. D. 1.75
Combination	36	9.64	
Lambs			
Phenothiazine	12	8.3	L. S. D. 1.88
Combination	12	8.2	

TABLE 3

Weight Gain Test in Feeder Cattle

Test Material	Number of Animals	Treatment Means (weight gains in pounds)	Analysis of Means
None (control)	80	32.38	L. S. D. 7.35
Phenothiazine	80	70.56	
Combination	87	84.98	

alone, and the results were highly significant when compared to the nontreated controls. Cattle receiving no treatment gained 32.38 lb. in 5 weeks. Those receiving phenothiazine suspension gained 70.56 lb., which was an additional 38.18 lb. over the nontreated control. The best gains were made by those receiving the combination, since they gained 84.98 lb. or 52.6 lb. more than nontreated controls and 14.42 lb. more than those with phenothiazine suspension.

Summary

A suspension containing 6.25 gm. of phenothiazine and 2.25 gm. of 2-2′-dihydroxy 5-5′-dichlorodiphenylmethane per ounce was compared on an equal volume basis with a suspension containing 12.5 gm. of phenothiazine per ounce in sheep and cattle. On a critical test, based on necropsy results in sheep, the combination was as effective as the larger phenothiazine dose. In weight gain studies in sheep, the combination treatment produced significantly greater gains in the adult ewes and was as effective in the lambs as phenothiazine alone. In the weight gain study in cattle, the animals treated with the combination showed a highly significant weight increase over untreated controls and a significant increase over the phenothiazine treated animals.

Based on these trials, there is good evidence the combination of the 2 drugs produced a better anthelmintic response than the larger dose of phenothiazine.

ACKNOWLEDGMENT

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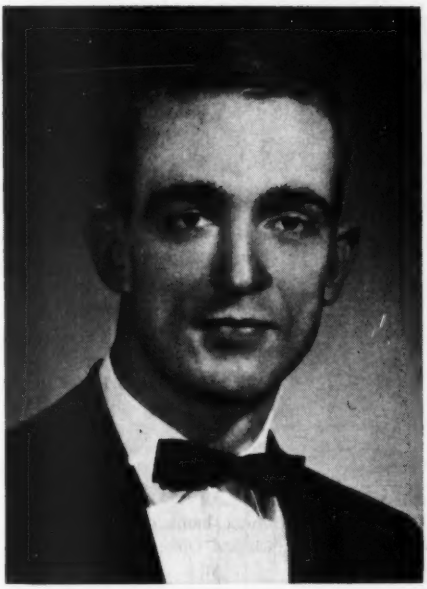
Practitioner's Laboratory

A Procedure for Assay of Thyroid Status in Animals

R. B. Wilson, B.S., D.V.M., W. M. Dickson, D.V.M., Ph.D., and F. N. Frost, D.V.M., M.S.
Washington State University

The estimation of thyroid function by standard clinical laboratory tests has failed to become popular in veterinary medicine. The measurement of metabolic rate in animals is a difficult, relatively inaccurate technic and subject to serious extrathyroidal influences. Blood cholesterol concentration, though reasonably simple to determine, is also inaccurate in that it is affected by conditions not related to thyroid dysfunction. Procedures involving the administration of radioactive iodine to the patient, though common in human clinical medicine, require bringing the animal to a laboratory which has the necessary special equipment. In addition, these latter technics are inconvenient, as radioactive wastes must be disposed of in accordance with Atomic Energy Commission regulations. Plasma protein-bound iodine measurement is an accurate reflection of thyroid function but is an expensive and relatively difficult technic.

This investigation was supported in part by the Mark L. Morris Animal Foundation and in part by funds made available by Biological and Medical Research through the State of Washington Initiative measure 171.



Dr. Robert B. Wilson received his D.V.M. degree in May 1961 from Washington State University. The studies were conducted as a senior research project.

A new test of thyroid function in man has recently been described.[1,2] This procedure involves the *in vitro* uptake of I^{131}-triiodothyronine (TRI) by the erythrocyte. The mechanism upon which this test operates is not fully known but it has been said to be a quantitative phenomenon related to the thyroxine binding capacity of the plasma.[3] As thyroid function increases or decreases, the available plasma protein sites occupied by the hormone decrease and increase respectively. The erythrocyte appears to be a secondary binding site for circulating thyroid hormone; thus, in hyperthyroidism, the excess hormone is associated with these cells while, in the opposite state of function, the hormone is almost entirely bound by plasma protein. The addition of labeled hormone to a sample of blood follows the same distribution. Therefore, increased or decreased thyroid output is reflected by increased or decreased radioactivity in or on the erythrocyte. (Modified procedures, utilizing ion exchange resins or urethane sponges rather than erythrocytes, have been described but are still in the developmental stage.[4,5]) This procedure has been shown to possess diagnostic accuracy comparable to other standard methods and eliminates many of the disadvantages of the earlier methods. Primary among these advantages is the lack of dependence on local diagnostic facilities. By the use of this technic, samples may be sent to distant diagnostic laboratories without undue distortion of values.

Materials and Methods

The standard procedure used in this study was the same as that described by other workers.[1,2] An aliquot containing 100 x 10^{-4} micrograms of Radio-L-Triiodothyronine I^{131}, (Triomet, Abbott Laboratories) was added to 3 ml. of oxalated or heparinized whole blood. The sample was then mixed by slow repeated inversion for 2 hours at 37.5 C. A 1 ml. aliquot was counted using a sodium iodide well-type scintillation detector and a 1 channel manual gamma spectrometer. The erythrocytes were then washed 5 times in physiological saline and recounted. Sufficient counts were recorded to allow for accuracy within 1%. The gross percent of TRI taken up by the erythrocytes was corrected to a standard packed cell volume (PCV) of 40.0 according to the following relationship.

$$\text{Percent uptake} = \frac{\text{Net counts/min. of erythrocytes}}{\text{Net counts/min. of whole blood}} \times 100 \times \frac{40}{\text{PCV of sample}}$$

TABLE 1

TWO HOUR UPTAKE OF TRI BY ERYTHROCYTES OF DIFFERENT SPECIES PER 40 PCV

Species	Class	Number	Percent Uptake High Value	Percent Uptake Low Value	Mean Value
Horse	All	37	29.40	10.00	17.68
Horse	Chronic Laminitis	4	15.90	10.00	12.25
Horse	Clinical Goiter	1	—	—	11.30
Cow	All	35	13.70	3.75	7.06
Dog	All	52	29.00	9.25	18.34
Dog	Clinical Hypothyroidism	3	12.80	9.25	11.12
Pig	Adult Sows	4	20.50	13.10	17.70
Cat	Adult	5	32.20	19.00	25.90
Sheep	Adult Ewes	10	4.90	3.90	4.52

Measurement of total blood cholesterol and the *in vivo* uptake of I^{131} by the thyroid are conventional assays of thyroid function and are compared with the TRI uptake procedure for correlative purposes.[6,7] Animals surveyed were clinical patients in the veterinary hospital or were from experimental projects within the College of Veterinary Medicine.

Results

No major technical difficulties were encountered in the performance of the standard procedure. Duplicate samples were noted to show differences of 0.0% to 4.0% for all species tested.

Reproducible results could be obtained from blood held in refrigeration for 10 days or at room temperature for 4 days, with no special precaution taken to insure sterility. Frozen plasma was tested over a period of 200 days by mixing it with fresh erythrocytes. Results from this experiment indicated that values vary up to 20% from fresh whole blood values but that results generally fall into the same diagnostic range.

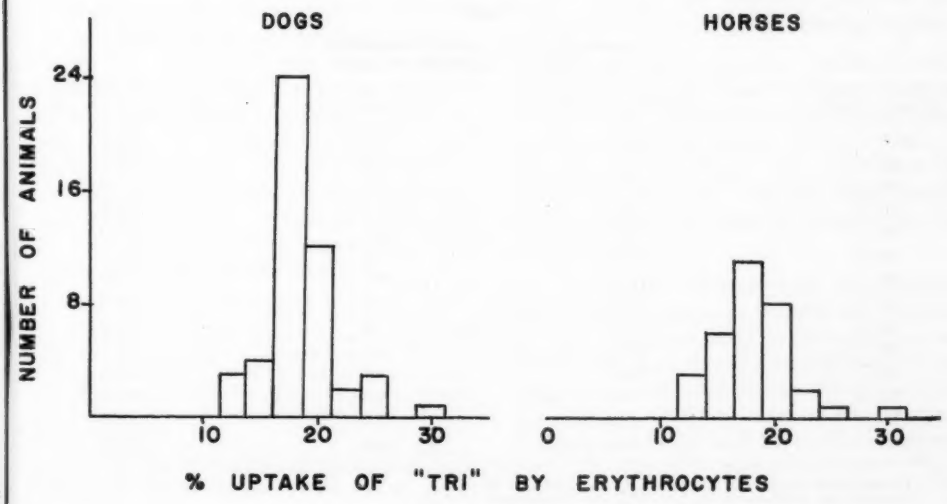
Preliminary results in our work indicate that there are distinct differences in the uptake and binding of TRI to the erythrocytes of different species.

Table 1 is a summary of values obtained in this study for the horse, cow, dog, pig, cat and sheep. All values have been corrected to the standard PCV of 40.0.

Values obtained for cattle appeared very uniform in distribution from the lowest to the highest values. The distribution of the values for dogs and horses is reported in Figure 1.

FIGURE 1

FREQUENCY DISTRIBUTION OF "TRI" UPTAKE BY NORMAL DOGS AND HORSES



Duplicate samples from 28 dogs were tested by means of the TRI uptake by erythrocytes and total blood cholesterol. The correlation coefficient (r) for this group was 0.70. Better correlation was noted between animals with high cholesterol levels than those with low cholesterol levels. It was noted, however, that in certain experimental animals undergoing changing states of thyroid function, the blood cholesterol levels were very unpredictable. This suggests that cholesterol levels depend on many factors which are not easily observed clinically.

The TRI uptake, standard I^{131} uptake, and total blood cholesterol were compared in 14 dogs. The results are reported in Table 2. All animals were young adult Beagles except for animal number CC-3, which was a 2-year-old male of mixed breeding and animal MC-11, which was a 6-year-old female of mixed breeding. All appeared to be normal and healthy except animal number MC-13, which had never exhibited signs of estrus and was obese.

Four horses with clinical diagnosis of chronic laminitis were tested. Their TRI uptakes were 10.0%, 11.4%, 11.7% and 15.9%. One horse was tested whose thyroid was by clinical examination enlarged 2 times normal size. The uptake of this animal was 11.3%.

Three dogs, clinically diagnosed as hypothyroid, had the following TRI uptakes of 9.25%, 11.3% and 12.8%.

The cat, pig and sheep have been surveyed in fewer numbers. Information obtained from these species suggests that mean uptake in the cat is quite high, exceeding that of the dog. Pig uptakes were similar to those of the horse and dog. Sheep appear to have values somewhat lower than the cow.

Discussion

No attempt was made in this study to evaluate the effects of certain drugs and various states of physiology on the uptake of TRI in animals. It was noted, however, that the highest values from the dog, cow and horse were recorded from individuals suffering from chronic debilitating diseases or malnutrition. Based on the number of animals tested, no significant differences could be found between animals of different sexes, ages, or breeds within a given species.

Of all horses tested the 4 lowest values were from 3 animals suffering with chronic laminitis and 1 animal whose thyroid gland

TABLE 2

CORRELATION OF THREE PARAMETERS OF THYROID FUNCTION OF DOGS

Animal Number	TRI Uptake (%)	I^{131} Uptake (%)	Total Cholesterol (mg.%)
CC-3	21.0	23.9	130.0
MC-2	18.2	4.6	147.0
MC-10	17.9	11.3	126.0
MC-8	16.9	12.4	158.0
MC-6	16.9	11.6	168.0
MC-9	16.2	11.6	147.0
MC-7	15.6	18.8	137.0
MC-13	15.1	11.8	211.0
MC-1	15.1	3.8	232.0
MC-12	14.1	6.3	211.0
MC-3	13.7	3.5	242.0
MC-4	12.6	4.9	174.0
MC-5	12.2	1.0	286.0
MC-11	11.3	0.0	430.0

Correlation coefficient (r) for TRI vs. $I^{131} = 0.76$.
Correlation coefficient (r) for TRI vs. Cholesterol = 0.72.

was by clinical examination, enlarged 2 times normal size. It has been recently reported that many cases of chronic laminitis in the horse are signs of a hypothyroid state.[8]

Three canine patients in the hospital demonstrated the lowest uptakes and showed many of the signs ascribed to the hypothyroid dog.[9]

The correlation between TRI and other parameters of thyroid function in the dog appears to be good for the dogs tested. One notable exception is number MC-2 listed in Table 2.

It is known that the plasma is the determining factor for variation of uptakes within a species,[1,2] but our results would indicate that the wide variation in uptake of TRI among the different species is due to the erythrocytes.

Summary

A new test of thyroid function in animals has been presented, utilizing *in vitro* uptake of I^{131}-L-Triiodothyronine by the erythrocytes. Stability studies on whole blood and plasma indicate that this test would be adaptable to conditions associated with veterinary practice. These conditions would include the necessary mailing or transportation of samples to suitably equipped laboratories.

Wide variation exists between the uptake of TRI among the various species. Horses and dogs otherwise diagnosed as hypothyroids possessed the lowest uptakes of the animals tested in these species. A good degree of correlation between the standard I^{131} uptake, total blood cholesterol and TRI uptake is reported for 1 group of dogs. High uptakes of TRI in the horse, dog and cow have been associated with chronic malnutrition and debility.

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Coccidiosis Control

Control of coccidiosis, a parasitic disease that costs livestock and poultry owners 50 million dollars per year, is in the offing.

Drs. John C. Lotz and R. G. Leek, parasitologists with the U. S. Department of Agriculture, reported in Washington that the attack on coccidiosis will be double-barreled. One method consists of giving drugs to animals before they get the disease; the other will be the spraying of fields where diseased animals have been.

The object of both technics is to disrupt the normal life cycle of the parasite as it passes through the digestive tract of one animal, to the field and into another animal.

The infective, egg-like, coccidial cysts, picked up from the field in forage, feed or water, can hatch inside the host animal only under certain conditions. If the shell of the cyst is not broken at the right time by the action of enzyme and bile, the parasite cannot mature and produce another generation of cysts.

Drugs that interfere with hatching action could be used to control the parasite within the animal host, the investigators reported. Enzyme-like sprays that destroy the shell of the cyst and expose the parasite to the elements could be used to kill off cysts lying in the fields, waiting to be swallowed.

Science News Letter, 79:255, (April 22) 1961

Equine Practice

Observations and notes on equine practice gleaned from 40 years of veterinary experience
by A. H. Quin, D.V.M.

The right ensemble for occurrence of "big head" or grazing edema is one or more short or long yearling colts, a warm spring day and a lush green pasture.

Turned to new grass after a period of stabling, the colts graze steadily, rarely raising their heads. The next morning, when the owner looks at the colts, he is severely shocked, for his cherished colts have heads that more nearly resemble that of a hippopotamus; even their lower lips are badly swollen.

If the colts are gentle and halter broken, they may be tied short at the manger for a couple of days. Two tablespoonfuls of sodium thiosulfite in their drinking water gives the groom or owner a nursing chore, even though no "miracle drug" claims can be made for this frightening, but so far as we know, never fatal abnormality.

For the owner's benfit a little well-worded advice on the prophylaxis of "big head" is in order. Turn green colts to their first grass gradually for a few hours only the first day and increase grazing time gradually to a full day on pasture.

Tetanus Aftercare

When a tetanus case takes a turn for the better and trismus has abated, pass the stomach tube and rinse the stomach with a few gallons of cool water containing ½ lb. sodium bicarbonate.

The return flow yields a surprisingly fetid accumulation of gastric debris and mucus. Then, while the tube is in place, pump in a gallon of oatmeal gruel. This simple procedure materially shortens the convalescent period and you can sense the gratitude of an appreciative patient.

Quidding

Practice with horses long enough and you will encounter a trouble the old timers called "quidding." Pathologically, the term describes unilateral or bilateral pharyngeal paralysis of central origin in aging horses.

History is that the owner finds "quids" or boluses of chewed hay in the feedbox or manger. You agree with him that some dental defect needs attention. But after floating and a molar check, the owner reports a week later that the horse is still dropping quids.

On the return trip you learn that the animal won't "flesh up" and, in fact, has been going down hill for several months. You toss him a handful of oats; he eats them but extends his head to swallow. Palpation of the throatlatch prompts a cough. There is some salivation and a light nasal discharge. In some of these cases, faulty innervation of the esophagus results in repeated choke.

The prognosis is always guarded and death may occur in from a few weeks to a year or more. Treatment includes soft mash grain mixtures and chopped hay, daily application of a good warm liniment over the pharynx, spaced weekly courses on an iodide and either ACTH or your corticosteroid of choice to effect.

African Horse Sickness: A Capsule Review

African horse sickness has decimated the equine population of many countries of Mid-Eastern Asia. The Southern part of Iraq is reported to have lost over 200,000 head of horses by mid-June, 1960. There are some 3,000,000 horses in the directly infected and exposed areas.

We hope it won't but it could occur here. So keep these highlights in mind.

Cause: A filtrable virus of several identified strains which do not cross immunize, or do so only weakly.

Susceptibility: All ages, but rare in suckling foals. Mules and donkeys more resistant. Recovered animals are actively immune.

Morbidity: Up to 100% in susceptible areas.

Mortality: 50 to 75% under treatment.

Vectors: Primarily by Culicoides gnats, but to some extent by mosquitoes and tabanids.

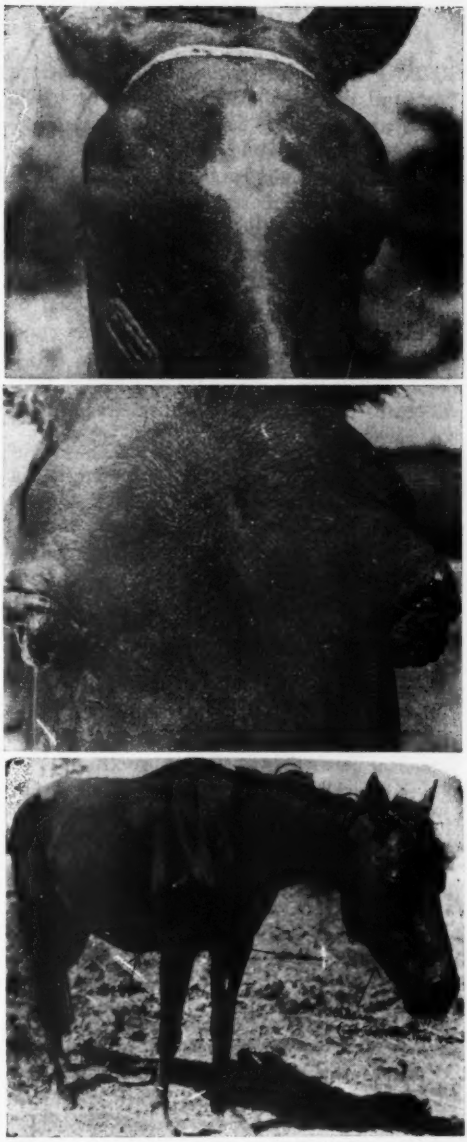
Incubation: Five to 7 days.

Symptoms: Temperatures 104 to 106 F. Progressive weakness, leucopenia, weak pulse, edematous swellings around eyes, head or trunk. Terminal pulmonary edema, coughing, and expulsion of yellow-white foam. Lymph glands swollen. Sheath swollen. Final decumbency and death in 6 to 8 days. A few paracute cases will die within 3 days. Subacute cases develop more slowly and some will begin recovery by end of 2nd week.

Differentiation: Longer incubation period, blood clots and no large, black, mushy spleen as in anthrax. In A.H.S. gelatinous pleuritis and pulmonary edema but hemorrhages more discrete.

Diagnosis: Can be specific by serological test against blood virus samples. Should contact A.R.S. for details.

Vaccination: With tissue culture or chick embryo vaccine, but must be strain-specific or polyvalent.



Top. Clinical symptoms of African Horse Sickness on 2nd day. Note increased fossa edema causing eyelid edema, ectropion and ocular discharge. Center. By the 4th day there is increased tissue edema and ulceration of conjunctival membranes. Bottom. General view of the horse. The animal died on the 5th day. Photos, courtesy of The Journal of the Royal Army Veterinary Corps, Aldershot, England.

Practice Tips

Acute Founder: In acute laminitis, bed a box stall deeply, induce the patient to lie down and pull the shoes. Plastic grocery bags containing some cracked ice secured with a not too tight rubber band and placed over each hoof will reduce congestion. Administer a light cathartic, an optimum dose of parenteral antihistamine and 10 minims of fluidextract of aconite (if you can still find any). Strip 150 cc. of whole blood or normal horse serum subcutaneously and give 2 gm. Butazolidin twice daily for 3 days. When the horse is up and better, trim the soles thin and give him the run of a soft, grass pasture for a week.

Navel Ill Prophylaxis: Supplementing proper attention to the recently severed cord, a liberal intramuscular dose of repositol penicillin is a good hedge against navel ill.

Tetanus Prophylaxis: Every colt up for castration merits 1,500 units of tetanus antitoxin.

Cutting the Haws: In some rural districts a horse owner may still request "cutting the haws" (membrana nictitans) to prevent moon blindness. Any veterinarian who complies with such a request should have his license revoked.

Some Causes of Lameness

Contracture of the Flexor Tendons of the Carpus

Etiology: May be congenital in the newborn foal or may follow navel infection. In older horses continued hard work on hard surfaces may be the cause.

Symptoms: Inflammation and indefinite swinging leg lameness with a shortening of the 2nd phase. The swelling and pain is acute, followed by a gradual thickening and contracture. In about 1 month the knee is bent.

Prognosis: Guarded, especially in old cases. The acute inflammation often recurs and becomes chronic.

Treatment: The acute is treated with rest and hot applications. If the horse must work, apply cold packs twice a day. For the newborn foal, place the leg in a cast and put on a high level of antibiotics, after nicking the tendons under a general anesthesia.

Thoroughpin

A dilatation of the bursa under the superficial digital flexor tendon just above the hock.

Etiology: It may be caused by a mild, chronic inflammation.

Symptoms: A painless swelling that can be pushed from side to side. There is no lameness.

Prognosis: Unfavorable.

Treatment: Aspirate fluid and inject the bursa with cortisone. In the past a pressure pack has been used, and tight bandaging with extreme flexion to rupture the bursa has been tried.

Corns

Etiology: A condition caused by a bruise but predisposed by thinning of the sole. It most commonly follows shoeing. The true corn occurs between the bar and the wall of the hoof.

Symptoms: A supporting leg lameness. Tenderness exhibited with hoof testers and paring of the sole will reveal the corn.

Prognosis: More favorable, if quite recent.

Treatment: Pare the sole to remove pressure and prevent further injury. This is accomplished by packing and shoeing until the hoof wall has grown down.

Quittor

A necrosis of the lateral cartilages.

Etiology: Mechanical injury to the lateral cartilage.

Symptoms: A fistula with discharge of pus to the outside at the coronary band. Lameness varies.

Prognosis: Fair unless there is lameness with it, then it is poor. It will take 3 months or longer to correct.

Treatment: Surgery to remove the lateral cartilage and all necrotic tissue. It may be necessary to operate more than once.

Comparative Study of Canine and Human Dermatology

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The purpose of this communication is to present a clinico-pathologic survey of canine benign and malignant melanomas and to compare these lesions to human counterparts. Our goals in comparative oncology have been described in previous reports.[1,2]

Definitions

The term "melanoma" in human medicine indicates a malignant growth; the prefix "malignant" is redundant. In veterinary literature, "melanoma" frequently is used generically without division into benign and malignant categories. This distinction is important to any study involving both disciplines. In order to avoid confusion and provide common ground for discussion, the following definitions apply in this communication:

1. *Melanocyte* ("clear cell")—mature melanin-producing cell.
2. *Benign melanoma*—refers to the pigmented nevus, a benign melanocytic tumor.
   a. *Junctional type* — melanocytes limited to epidermal-dermal junction, junctional nevus.
   b. *Compound type* — melanocytes at epidermal-dermal junction and in dermis, compound nevus.
   c. *Dermal type* — melanocytes in dermis only, dermal nevus.
3. *Malignant melanoma*—refers to the malignant melanocytic tumor.
4. *Melanoma*—used generically to apply both to benign and malignant melanoma.
5. *Blue nevus*—a benign melanocytic tumor principally of the dermis (subcutaneous tissue may be involved); component cells thought to have failed to complete the migration from the neural crest to the epidermal-dermal junction.

Dr. Orkin

Supported in part by a grant from the Minnesota Division, American Cancer Society, Inc.

6. *Cellular blue nevus*—variant of blue nevus, distinguishable histologically.

Cutaneous benign and malignant melanomas are common in most animal species.[3] Their incidence in grey horses is striking; they are comparatively rare in horses of other colors.[4] The equine tumors are virtually unknown in animals under the age of 6 years; rise to 36% incidence at 8-10, 61% at 10-12 and 80% beyond 15 years. Some of the neoplasms are highly malignant and metastasize widely.[5]

Mulligan[6] reported 4.2% of 1,000 canine neoplasms of all organs were melanomas; 2.4% benign; and 1.8% malignant. An enigmatic problem is the apparent difference in incidence of oral malignant melanoma in America and England. While this tumor appears to be the most common canine oral malignancy in this country, with the squamous-cell carcinoma a poor second,[7] the reverse seems to be true in Britain. Gorlin and co-authors[8] noted 20% of their series of canine oral neoplasms were malignant melanomas (the most frequent malignant tumor), while only 5.5% were squamous-cell carcinomas.* In contradistinction, Cotchin,[9] obtaining material from the Royal Veterinary Pathology Department (London), presented a series, 50% of which consisted of squamous-cell carcinomas and only 16% of malignant melanomas.

The majority of canine cutaneous melanomas are benign;[6,10] however, Gorlin and associates[8] reported the vast majority of oral melanomas were malignant (18:1 ratio).

Smith and Jones were of the opinion that malignant melanomas in animals do not develop from benign melanomas, as is frequently stated in reference to man. Mulligan,[6] however, believed that an irritated or incompletely excised, apparently benign melanoma in the dog may be transformed into a malignant lesion (he presents no objective proof of this).

Canine melanomas are reported to predominate in males, particularly in the Terrier and Springer Spaniel breeds. Sastry[11] considered that canines with heavily pigmented skin are more susceptible to melanomas, in contrast to humans where lightly pigmented individuals are more susceptible. This statement requires qualification since in man it is malignant melanoma (not all melanomas) which is reported to predominate in patients with fair skin. Canine melanomas have their highest incidence in the 7-14 year age group, human equivalent (H.E.), 44-72 years. The tumors tend to involve the head (particularly the lip, eyelid and perioral areas), trunk, and extremities. Kral and Novak[12] stated that canine "amelanotic melanomas are very common."

Cotchin[10] divided the canine cutaneous melanomas of his series in 3 categories: malignant, benign cellular and benign fibrous. Many cases of the first type correspond to the malignant melanoma of the present discussion (numerous mitoses in histologic sections, metastases identified in all subjects autopsied, etc.). Study of photomicrographs presented suggest that some of the non-metastasizing tumors may actually be blue nevi, similarly certain of the metastasizing lesions have areas suggesting remnants of cellular blue nevus tissue. The second type corresponds to the benign melanoma. The third probably is a blue nevus.

Cotchin described malignant melanoma as a variably-pigmented (usually dark) tumor, of the deep cutis, which invades underlying tissues and overlying epithelium, producing ulceration. Noteworthy was the frequency of scrotal involvement in malignant cases, and digital localization in the benign cellular type. Benign melanomas are hemispheric, dome-shaped or pedunculated, dark tumors of the cutis.

Within weeks or months, canine malignant melanoma may invade contiguous tissue or matastasize via lymph and/or blood stream to the lungs (the most frequent site), spleen, kidney, brain, etc.

**The material for Gorlin and co-authors' initial study was collected from the files of the surgical pathology division of the University of Minnesota Veterinary school and is therefore similar, in general, to the material of the present study.*

Therapy consists of prophylactic excision of benign melanomas and wide surgical removal of malignant melanomas with draining lymph nodes and vessels. Follow-up of these patients is extremely difficult and therefore 2-year survival periods are not quoted. If the condition is widely disseminated, euthanasia frequently is performed.

Microscopic study of benign melanoma reveals polyhedral cells, grouped in solid masses, alveolar patterns, or larger compartments, with single oval or round nuclei and a variable amount of melanin in the abundant cytoplasm. Spindle-shaped and tapered slender cells occur in sweeping bundles resembling proliferated nerve sheath cells.[13] Cells are close together with fairly frequent whorling resembling Meissner's corpuscles.

Histologic study of malignant melanoma reveals a preponderance of polyhedral and stubby spindle cells in loose, irregular compartments. There is no tendency to resemble nerve sheath tumors. Cells tend to be larger than those of benign melanoma and may contain little or no melanin. Nuclei vary greatly in size, with some giant and bizarre forms present. Nucleoli may be prominent and bizarre mitoses may be present. The histology of metastatic lesions is similar to that of the primary.

Mulligan[8] stated that "so-called junctional change has not been observed in any melanoma" (canine—note). Cotchin[10] remarked that "no definite origin of the tumor cells from the epidermis can be seen, although in occasional places the appearances are quite suggestive of this." Gorlin and co-workers[14] noted 20% of oral malignant melanomas examined by them showed typical junctional changes adjacent to the tumor (Fig. 1); junctional nests were also observed in oral benign melanomas.

The neural crest origin of canine melanoma cells has not yet been demonstrated; however, Lennox[15] stated: "It seems improbable that a process established with such consistency in the rest of vertebrate phylum, occurring at a stable phase of embryonic development when species differences are minimal, has been fundamentally altered during the evolution of the mammal."

Fitzpatrick and associates[16] reported an active tyrosinase system in equine melanomas similar to that of man. There has been no comparable canine study.

In 1938 Passey[17] reported experimental production of malignant melanoma in the dog. He applied tar once weekly to the dorsal cervical region of 9 Airedale bitches. At the end of 7 years, 3 had developed tumors—one undoubtedly, and another probably, malignant melanoma. The tumor of the 3rd dog was deeply pigmented but awaited microscopic confirmation. This study is particularly significant since the canine is known to be resistant to induction of tar cancer (spinocellular).[18]

Materials and Methods

One hundred cutaneous tumors were collected from 90 dogs during a 1-year period (May 1957 to May 1958). There were 41 male dogs, 45 female (4 spayed)

Fig. 1. Canine and oral malignant melanoma—theques of tumor cells in the lower epidermis with some cells migrating upward to stratum malpighii; x175. (Courtesy of Dr. R. J. Gorlin, University of Minnesota, School of Dentistry).

and 4 in whom sex was not known. Sixty of these dogs (70 tumors) were examined clinically at the University of Minnesota Veterinary Clinic. In an additional 30 cases (30 tumors), tissue specimens with clinical data were submitted by veterinarians in the surrounding area. A majority of the patients at the veterinary clinic were presented because of cutaneous tumors; the rest of the tumors were discovered during examination for some other condition.

A complete physical examination was done on all clinic animals. A punch or excision biopsy was performed on one or more tumors in each of the dogs. Touch smears and bleeding and clotting time were determined in those cases in which mastocytoma was suspected.

Punch Biopsy—Hair was removed with scissors and the site anesthetized with Frigiderm (Brachvogal-Hovey, Los Angeles, California). A punch biopsy was performed and the tissue fixed in 10% buffered formalin for at least 24 hours. Hematoxylin-eosin and toluidine blue stains were performed in the usual manner on all tumors. Specimens from cases of transmissible reticulum-cell tumor were stained with Foot's modification of Bielschowsky's method.

Excision Biopsy — This was accomplished under general anesthesia (pentobarbital sodium), and the tissue fixed and stained as above.

Touch Smears—A dry, clean slide was pressed gently against the freshly cut surface of the excised tumor. The slide was allowed to dry and was stained with Wright's stain. Purple-red granules in cells 8-18 microns in diameter were considered diagnostic of mast cells.

A previously presented statistical correlation[3] of the age, breed and sex distribution of our total tumor series to a "sample normal population" revealed:

1) Very few affected animals were under one year of age (H.E., 15 years).
2) Nearly one-half of the "tumor" population was over 9 years of age (H.E., 52 years).
3) The vast majority of malignant conditions occurred in animals 9 years of age or older.
4) The general tendency to cutaneous neoplasia appeared to be independent of major breeds and sex of the "sample normal population."

Authors' Observations

Melanomas comprise 9% of our tumor series, 7% benign and 2% malignant. Malignant melanoma provides 50% of carcinomas and 29% of the total cutaneous malignancies (10% if mastocytoma is considered malignant). The present authors had previously commented that canine mastocytoma is not necessarily a malignant condition.[1]

Clinical study of the dogs with benign melanomas reveals: A mean age of 4.5 years (H.E., 34 years) with 3 dogs one year of age (H.E., 15 years); 40% of cases involving mongrels (2 out of 5 dogs), 60% occurrence in males (3 out of 5 dogs). The clinical appearance of lesions ranged from black macules (Fig. 2) to hemispheric amelanotic or dark nodules (Fig. 3). Therapy consisted of local excision; no recurrences were known at the time of publication.

Statistical correlation of the age of dogs having benign melanoma with that of the aforementioned "sample normal population" showed the condition to be relatively more frequent in younger dogs (X^2 Yates Correction = 9.661, $P = < .01$). The analyses of sex and breed, where these factors were known, yielded frequencies too small to be statistically significant.

The dogs with malignant melanoma were both male, a 9-year-old Cocker Spaniel and an 8-month-old Chihuahua. Because of the young age of the latter dog (H.E., 12 years) the diagnosis of juvenile melanoma had been considered despite the absence of distinctive tumor giant cells found in 50% of human cases.[10] Juvenile melanoma has not been delineated in dogs. The lesion was described by the referring veterinarian

Fig. 2.

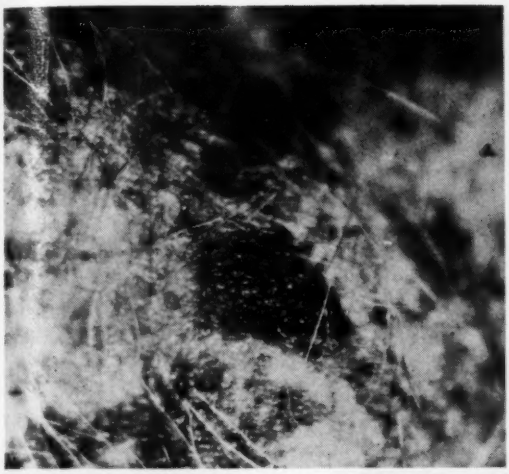
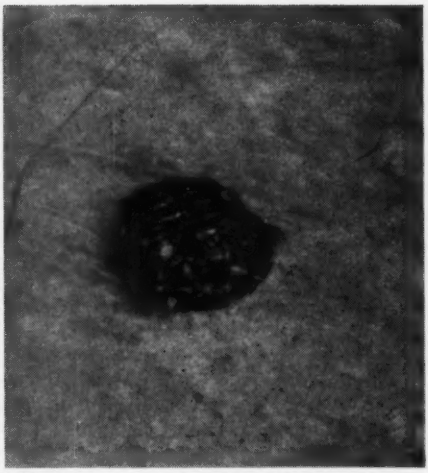


Fig. 3.



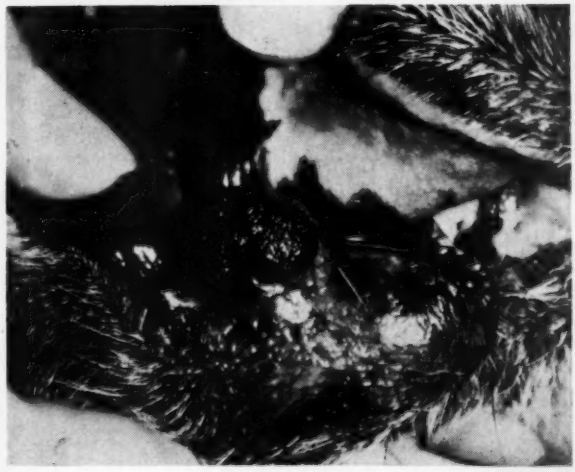


Fig. 4.

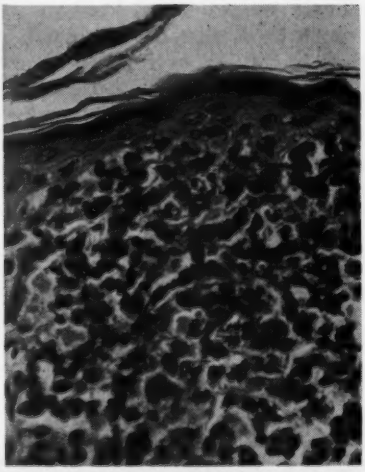


Fig. 6. (center, right)

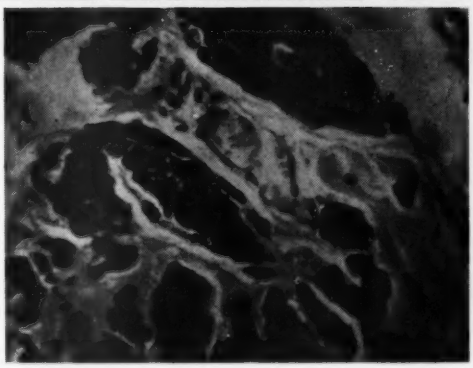


Fig. 5.

Fig. 2. Canine cutaneous benign melanoma—black, irregular macules on scrotum.

Fig. 3. Canine cutaneous benign melanoma—Blue-black nodule on flank.

Fig. 4. Canine cutaneous malignant melanoma—ulcerated, black nodular lesion of lower lip. Recurred after wide excision and metastasized to lung.

Fig. 5. Canine cutaneous benign melanoma—nests of tumor cells with abundant melanin obscuring cell detail; x330.

Fig. 6. Canine cutaneous benign melanoma (compound type)—melanocytes (single and groups) "dropping off" epidermal-dermal junction; x450.

as a 2 cm. (diameter), erythematous, dome-shaped tumor on the carpal area. There has been no recurrence following local excision. The lesion of the Cocker Spaniel was an eroded, black, nodular tumor fixed superficially to the lip (Fig. 4). It recurred 2 weeks after operation (wide excision with contiguous lymph node dissection), and metastasized to the lungs. The dog was euthanized but permission for postmortem examination was denied.

Statistical analysis of age, breed and sex of the dogs having malignant melanoma is not presented because of the low value of the sample.

Microscopic examination of the benign melanomas showed nests and cords of polyhedral cells with oval, vesicular nuclei and abundant eosinophilic cytoplasm. Melanin content ranged from scant to abundant enough to obscure nuclear detail (Fig. 5). Four of the lesions were of the compound type; the remaining 3 of dermal type. There was no constant correlation between clinical, *e.g.*, flat or nodular lesions, and histopathologic, compound or dermal types. Junctional activity was usually limited to "dropping off" of individual cells and groups of cells from the basal layer (Fig. 6); in sereral lesions epidermal nests were noted (Fig. 7). There appeared to be a tendency for cells in the lower dermis to be fusiform (Fig. 8).

Histologic study of the malignant melanomas revealed large, discrete cells of varied outline (polyhedral predominating). As compared with the benign melanomas, there was much less grouping. Nuclei were large in relation to cytoplasm. They varied greatly in size and shape, had frequent and bizarre mitotic figures and a single prominent nucleolus (Fig. 9). Melanin was absent or moderate; only occasionally did it obscure cellular detail. Cords and individual tumor cells were noted to be "dropping off" the basal layer; occasional epidermal nests were present (Fig. 10).

Our observations differed from those of the literature: the occurrence of flat, benign melanomas in addition to dome-shaped and nodular lesions previously described; the presence of a "dropping off" type of junctional activity and occasional epidermal theques, in benign and malignant lesions, and absence, histologically, of areas in benign melanomas resembling Meissner's corpuscles and proliferated nerve sheath cells.

Human Correlation

Incidence—The benign melanoma is the most common cutaneous neoplasm of

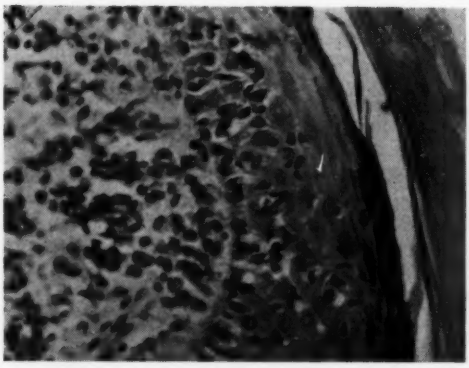


Fig. 7. Canine cutaneous benign melanoma (compound type)—note epidermal nests of melanocytes (lesion of ankle); x330.

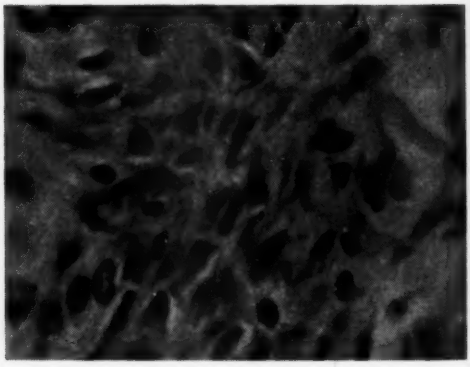


Fig. 8. Canine cutaneous benign melanoma—tendency of tumor cells to be fusiform in lower dermis; x720.

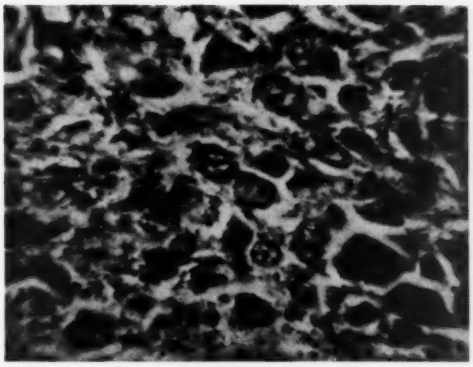


Fig. 9. Canine cutaneous malignant melanoma (photomicrograph of case in Fig. 4)—tumor cells varying in size and shape with large nucleus and prominent single nucleolus producing a "bird's eye" effect; x330.

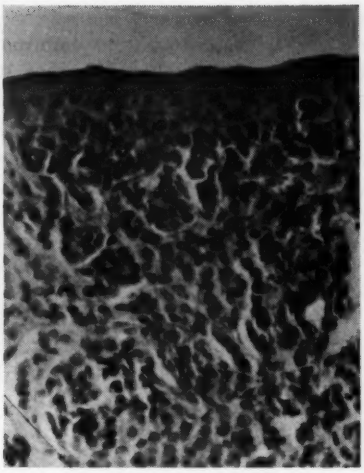


Fig. 10. Canine cutaneous malignant melanoma—melanocytes (single and groups) "dropping off" epidermal-dermal junction, occasional epidermal theques also present; x330.

man.[20] Every adult has a few to hundreds of such lesions, the vast majority of which remain benign. These neoplasms (usually flat lesions) in rare instances involve the stratified epithelium of the mouth and the mucocutaneous junction of the anus. Cutaneous benign melanomas accounted for 7% of our canine tumors and 12.1% of those of ectodermal origin. It is likely that they are even more common than these figures would indicate. Many dog owners will not consult veterinarians for such "insignificant" lesions, particularly when they are flat, asymptomatic, and covered by a thick hair coat. At any rate, cutaneous benign melanomas are common in both species.

Ackerman and del Regato[21] noted malignant melanoma comprised 2.9% of malignant cutaneous tumors of man. In the present series malignant melanoma included 29% of malignant tumors of the skin (10% if mastocytoma is considered malignant). Carcinoma of the human oral cavity is considered to be practically always of the squamous-cell type.[22] Allen and Spitz,[23] however, reported 5.9% of 337 malignant melanomas originated from structures of the oral cavity. Patients so afflicted have an almost uniformly fatal prognosis. Gorlin and co-workers[8] observed almost 4 times as many malignant melanomas as squamous-cell carcinomas in the canine oral cavity. It seems, from admittedly small canine samples, that mucocutaneous malignant melanoma is relatively more common (compared with other mucocutaneous cancer) in the canine than in man.

Genetics—The tendency to form benign melanomas in the human appear to be partially under genetic control.[24] In some fish, gray horses, and other animals, malignant melanoma is transmitted genetically. In the human, only once has cutaneous malignant melanoma been described in more than one member of a family (father, son and daughter), although there have been 4 reports of malignant melanoma of the eye in families.[25] We know of no reports of genetic factors in canine benign and malignant melanomas.

Clinical aspects—Data on age, sex, site predilection and clinical appearance of canine melanomas is frequently presented without division into benign and malignant categories; thus, such comparative information on these topics is difficult to assess. From the present study, it appears that benign melanomas are relatively more common in younger dogs. Clinically, flat, hemi-

spherical, and nodular benign lesions were noted. It is obvious that information accrued from such a small series can only permit impressions rather than conclusions.

In man, benign melanomas are uncommon before the age of 2 years; they usually commence in early childhood as flat, pigmented lesions (junctional type). Junctional activity is most frequent and of greatest intensity in the first decade, whereupon it rapidly diminishes.[26] The development from a junctional into a compound and further into a dermal type appears to be a matter of aging. As a result of "dropping off" of melanocytes from the epidermal-dermal junction, the benign tumors become thickened and elevated. Lesions on the soles, palms and genitalia are exceptions to this sequence, since they are almost invariably of junctional or compound type even in adults. Benign melanomas darken and grow and new lesions appear at puberty and during pregnancy. At approximately the age of 30, canine equivalent, (C.E., 3½ years), these neoplasms may show decreased melanocytic activity and regress. By the 5th decade new lesions cease to appear. The tumors may disappear as a result of: (1) formation of pedunculated soft tags which drop off the skin due to friction and trauma; (2) fibrosis, and (3) fatty infiltration of quiescent atrophic nevi.[27]

Shaffer[28] correlated the clinical types of benign melanomas of man with the different histologic pictures. He divided these lesions into morphologic categories: (1) flat, (2) slightly elevated, (3) halo, (4) verrucoid, (5) polypoid, (6) dome-shaped, (7) sessile, and (8) papillomatous. The first group was composed almost wholly of the junctional type. The second and third consisted largely of the compound variety. The fourth group was comprised mostly of the dermal type with evidence of junctional activity, while groups 5, 6, 7, and 8 were almost exclusively dermal.

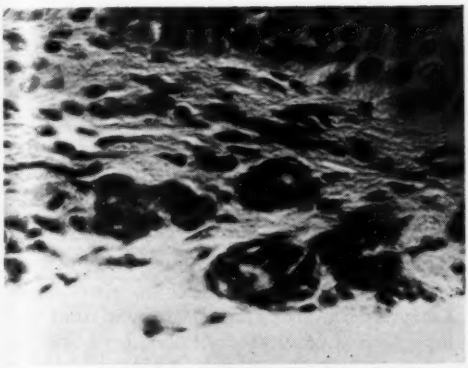
There is a great need for such correlative clinico-pathologic studies as the above in the dog, with emphasis on chronic changes in lesions from early life through senescence. This knowledge might help to substantiate the authors' impression that benign melanomas of dog and man are comparable.

Malignant melanomas in man account for approximately 1% of deaths attributable to malignant tumors.[24] Lesions predominate in the same age group as other carcinomas of the skin, that is, between 30 and 60 years of age (C.E., 3½-12½ years). Males and females are equally involved; however, the prognosis is much better in the female. The condition is 2 to 4 times more common in Caucasians than Negroes. The antithesis in the preferential involvement of malignant melanomas in heavily pigmented canines and lightly pigmented humans is inexplicable at present. In general, the lesions in man are prone to involve the skin of the head and neck, soles, rest of the lower extremities, upper extremities, and mucous membranes of the head and neck, in that approximate order. Malignant melanomas are believed to arise from pre-existing benign melanoma in over 50% of cases.[29] Metastasis may occur initially to the regional lymphatics and subsequently to the liver, lungs, brain, skin, etc. Allen and Spitz reported a 20% survival rate (5 years plus), 68% of which had been treated by wide local excision and the remainder by local excision plus lymph node dissection. Although the information pertaining to the canine lesions is somewhat incomplete, there are noted many similarities to the clinical appearance and behavior pattern of malignant melanomas in man.*

Histopathology — Microscopic changes in our canine cutaneous melanomas (benign and malignant) are comparable to those of man (Figs. 11-13) as described by Lever,[20] Lund and Stobbs, and Allen and Spitz, excepting the type of junctional activity. Epidermal theques of melanoma cells are common in human benign (junctional and compound types) and malignant melanomas. In the present study junctional

**There is an interspecies difference in the degree of pigmentation of benign melanomas; canine lesions tend to be darker in color (not uncommonly black or blue-black) than human counterparts.*

Fig. 11.



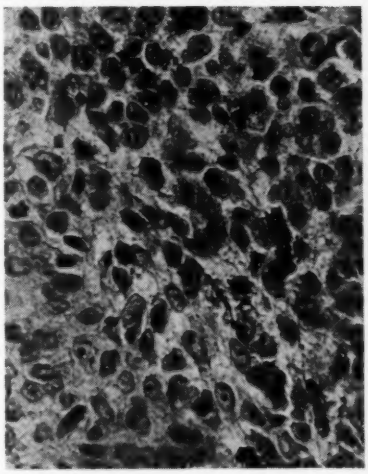


Fig. 13.

Fig. 12.

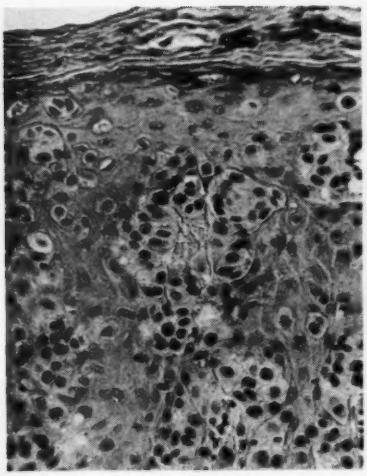
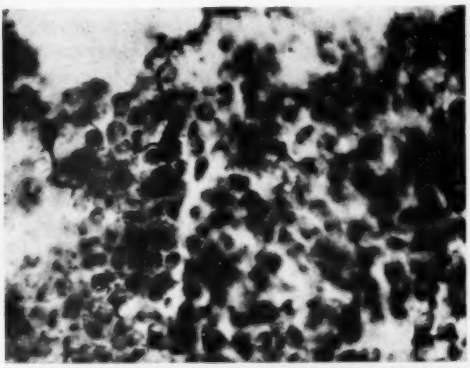


Fig. 14.



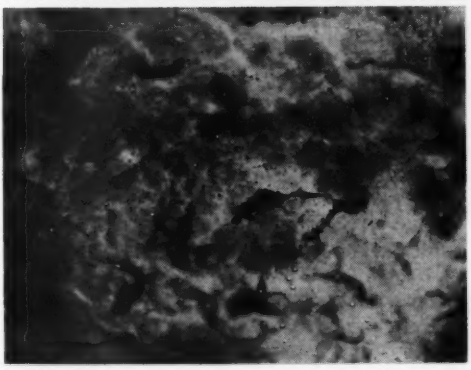


Fig. 15.

Fig. 11. Human cutaneous benign melanoma (dermal type)—intradermal nests of tumor cells; x330.

Fig. 12. Human cutaneous malignant melanoma—many epidermal nests of tumor cells, some penetrate to stratum corneum; x330.

Fig. 13. Human cutaneous malignant melanoma—tumor cells vary in size and shape. Prominent single nucleolus within large nucleus produces "bird's eye" effect (compare with Fig. 8); x330.

Fig. 14. Epidermal melanocytes — forehead of darkly pigmented canine (dopa stained following skin-splitting with trypsin); x400. (Courtesy of Dr. G. Szabo, Harvard Medical School, Department of Dermatology).

Fig. 15. Epidermal melanocytes — forehead of lightly colored canine (dopa stained following skin-splitting with trypsin); x400 (Courtesy of Dr. G. Szabo, Harvard Medical School, Department of Dermatology).

activity consisted mainly of "dropping off" of tumor cells (single or groups) from the epidermal-dermal interface. This interspecies difference is particularly important since in man it is considered that the first sign of malignant change in a benign melanoma occurs at the epidermal-dermal junction (with the exceptions of rare cases evolving from the cellular blue nevus[23] and nevus of Ota).[21] No true junctional nevus has been described in the dog. This is consonant with Stegmeyer's[22] contention that junctional nevi have not been reported in mammals (aside from man).

Canine Melanocytic System—It is pertinent at this point, to review what is known of the anatomy of melanocytes in the dog. Lovell[25] noted many clear cells (hematoxylin-eosin stains only) admixed with basal cells in the stratum germinativum of normal canine skin. He stated that in these cells the "cytoplasm appears completely transparent and the nuclei are extremely basophilic." The photomicrographs, accompanying his thesis, give an excellent demonstration of clear cells. They are more numerous in the thicker skin of the planum nasale (tip of nose) and foot pads than in the thinner skin of hairy areas. There is no increase in their number with age. In pigmented regions basal cells also contain varying amounts of pigment granules on the distal side of their nucleus. Although Lovell cited several salient references on the melanocytes in normal human epidermis, he preferred to designate the canine counterparts as "mitotic cells" (*sic*).

Szabo[24] utilized dopa stains on pure epidermal sheets (following skin-splitting with trypsin)of normal canine skin. He found epidermal melanocytes in the soles, palms, tail, external ears, nostrils and forehead (Figs. 14, 15); similar dermal preparations failed to demonstrate a dermal melanocytic system. This corresponds to the finding in most areas of the skin of postnatal man,[26] but differs from that of certain anthropoid apes (chimpanzee and orang) where melanocytes may be demonstrated in both the epidermis and dermis in practically all body regions.[26] As evidenced from the preliminary data cited, the melanocytic system of man and dog appear to have much in common.

Hypotheses—Possible explanations of the paucity of epidermal nests in canine as compared to human cutaneous melanomas are: A. Differences in epidermal anatomy between the 2 species produce an artificial division; B. Benign melanomas of the dog are comparable to blue nevi (or cellular blue nevi) of man and malignant melanomas arise therefrom; C. An intrinsic difference exists between melanomas of the 2 species.

A. Difference in Epidermal Anatomy—Early in the study we postulated that the infrequency of epidermal theques could be a function of the absence of the rete ridges. The evidence collated for this hypothesis is:

1. A striking interspecies difference in epidermal anatomy resides in the absence of rete ridges in hairy skin of canines.* The epidermis of nonhairy canine skin (tip of nose and foot pads) is thicker, has rete ridges and, as mentioned above, a greater number of clear cells. Oral mucous membranes contain rete ridges; their concentration of clear cells is not recorded. Oral benign and malignant melanomas (Fig. 1) show typical junctional nests of tumor cells. We have seen no examples of melanomas from the tip of the nose or foot pads, the only cutaneous regions normally possessing rete ridges. It would be of interest if melanomas in these areas showed prominent epidermal theques. The "dropping off" type of junctional activity observed in our subjects occurred mainly on hairy skin or transitional epithelium, sites where rete ridges are normally absent (rima ani a possible exception).[26]

**Interestingly, epidermal ridges are usually lacking in most laboratory mammals, such as the rat, mouse and rabbit. The skin of these animals is rich in hair follicles which may take the place of the rete ridges and papillae found in human skin.*[27]

2. The rete ridge system of man is much more highly developed than that of the dog. Dramatic patterns are formed in human palms, soles, genitalia, rima ani, lips, eyelids and hair-free margins of external ears (majority of above are hairless). Some of the areas listed have a relatively high incidence of malignant melanoma (importance of junctional activity stressed previously). Benign melanomas in the first 3 regions are exceptions to the usual evolution of such lesions on the general body surface, *i.e.*, they almost invariably maintain junctional activity even in the adult.

3. Melanocytes are reported to be more numerous on epidermal ridges in comparison to the valleys,[39,40] although Staricco and Pinkus[41] believed that this differential is accentuated by the laws of optics. Szabo[40] has postulated that the regional distribution of human malignant melanoma may be primarily due to differences in population densities of melanocytes.

4. The presence of hair in a human benign melanoma is strong presumptive evidence that the lesion is dermal in type (no junctional activity or malignant potential).[43] On the other hand, the junctional type of benign melanoma is usually hairless.

It is tempting to speculate that the prominence of epidermal theques in melanomas bears a relationship to the presence of rete ridges in the normal anatomy of the affected site. Whether this is a function of the predominant ridge localization of melanocytes is problematic. A reciprocal relationship exists between the presence of hair follicles and rete ridges in the normal skin of certain animals. A further corollary is the possible pre-eminence of junctional changes in hairless areas (more extensive ridge pattern?) of man and dog.

Evidence against this concept:

1. Fortner and Allen[45-48] investigated the spontaneous development of malignant melanoma in 2% of a large colony of Syrian (golden) hamsters. These transplantable tumors predominated on the skin of the neck and trunk.* Microscopic epidermal changes were identical to those of man (loss of cohesion, features of anaplasia, etc.) excepting the absence of pseudoepitheliomatous hyperplasia. Rete ridges are present only in the soles of the normal skin of the hamster.[48] The presence of typical epidermal alterations of malignant melanoma in an animal with a rete ridge pattern approximating that of the canine offers phylogenetic evidence again the hypothesis advanced above.

2. Epidermal nests of tumor cells were observed in a benign melanoma on a hairy region (ankle, Fig. 7); control sections from normal ankles of dogs of the same breed (unfortunately not the affected animal) showed no rete ridges.

The evidence, therefore—although suggesting a possible association between rete ridges and epidermal theques of melanoma cells—is inconsistent, in part, and preliminary at best.

B. Comparability to Blue Nevi (Typical and Cellular). The blue nevus in man is a benign, dermal, melanocytic tumor usually present at birth or developing shortly thereafter.[46] Typically, a single, blue to blue-black papule or nodule is present on the dorsal surface of an extremity. The component cells are thought to represent melanocytes that failed to complete their migration to the epidermal-dermal junction. The Mongolian spot, nevus of Ota and blue nevus are considered to be closely related,

**The authors asserted that the tumors originated from junctional nevi, and the latter were also found in hamsters unaffected by malignant melanoma. Stegmeyer[33] questioned these findings and suggested that the tumors may have arisen de novo from the epithelium.*

and possibly represent different stages of the same process. Histologically, the blue nevus consists of compact or loosely disposed fascicles of elongated spindle-shaped cells containing much melanin. The lesions are generally located in the lower two-thirds of the dermis; occasionally they lie directly against the epidermis.[47] This neoplasm is not likely to be confused with the more common dermal type of benign melanoma.

The cellular variant of the blue nevus is usually larger in size than the common type. It is characterized histologically by cellular islands resembling these of the dermal type of benign melanoma, but pale in contrast to the surrounding ordinary blue nevus tissue. As a result of the cellularity and abundance of melanin, this neoplasm is frequently misdiagnosed as malignant melanoma. Four cases of cellular blue nevi observed by Allen and Spitz[23] manifested apparently innocuous metastatic foci (well-differentiated) to regional lymph nodes. They also reported 6 cases of true malignant melanoma arising from cellular blue nevi.

Allen[47] considered that cellular blue nevi are common in grey horses; they are usually diagnosed erroneously as malignant melanomas. As opposed to true equine malignant melanoma, cellular blue nevi rarely metastasize.

As mentioned previously, some of the canine melanomas reported by Cotchin[10] (in Britain) are likely blue nevi (typical and cellular); in addition, study of photomicrographs presented suggests that several malignant melanomas had evolved from cellular blue nevi. Such examples were not uncovered in the present series, nor apparently —as far as can be determined from study of photomicrographs—in that of Mulligan[18] (in Denver). Whether this difference is geographic—as obtained for the ratio of oral malignant melanomas to to squamous-cell carcinomas—or artificial, due to the small size of the samples, is impossible to state.

Arguments against the comparability of the canine melanomas in the present series to blue nevi include:

1. Junctional activity — epidermal theques in occasional cases and the "dropping off" type in many—is incompatible with the diagnosis of blue nevi. However, in rare instances in humans, blue nevi have been reported in association with an overlying junctional nevus.[23]
2. In the dermal type of benign melanoma the cellular structure was not typical of the blue nevus (conventional or cellular).
3. If malignant melanoma developed subsequent to blue nevi, remnants of blue nevus tissue should persist. This was not observed.

Canine blue nevi (typical and cellular) do occur. They will likely be encountered wherever sought, as experience accumulates. However, they do not represent all canine melanocytic tumors, as is evidenced by the present study.

C. Intrinsic Interspecies Difference. The accumulated data presented in previous sections tends to refute this possibility.

It is our impression that canine benign and malignant melanomas are comparable to human pigmented nevi (excluding the junctional type which does not occur as such in the dog) and malignant melanomas, respectively. Further investigation (clinicopathologic, tyrosinase system, etc.) must be accomplished before this impression can be substantiated. Canine lesions analogous to human blue nevi (typical and cellular) exist; additional study may reveal that they are much more common than heretofore suspected.

Fitzpatrick,[49] in commenting on the similarity of the tyrosinase system and histologic appearance of the equine melanoma to that of the human, reported: "Horse melanoma, therefore, offers a unique opportunity to students of melanoma for a prolonged and careful study of the biology of melanoma as it occurs spontaneously in mammals. The technical difficulties associated with the large size of the animal, such as care and feeding, and difficulty in necropsy, have prevented a thorough study of this remarkable animal tumor." Many of the difficulties attendant upon the investigation of melanoma in the horse may be

obviated by the study of these tumors in the smaller and more available canine.

Summary

Benign (pigmented nevus) and malignant cutaneous melanoma are relatively common in man and dog.

There are many similarities in the clinical appearance and behavior patterns of benign and malignant melanoma in the human and dog.

Pathologic characteristics of canine cutaneous melanomas (benign and malignant) closely approximate those of the human, with the exception of the type of junctional activity. In the canine, junctional changes are limited mainly to "dropping off" of cells (single and groups): occasional lesions show epidermal nests. This possibly bears a relationship to interspecies differences in epidermal anatomy. Malignant melanomas of the canine oral cavity not uncommonly have typical junctional theques and thus, histologically, may be indistinguishable from the human counterpart.

It would be premature to state that canine and human melanomas (benign and malignant) are completely analogous. There is need for intense clinico-pathologic study of canine benign melanomas from their incipience until they become quiescent.

Canine melanomas offer an unusual opportunity for the study of melanoma as it occurs spontaneously, and possibly experimentally (malignant variety), in an available mammal.

ADDENDUM

Subsequent to the preparation of the manuscript, 27 cases (Pathologic material and clinical data) of *melanoma* were drawn from the files of the University of Pennsylvania Veterinary School (Division of Pathology). This comprised all tumors filed under this heading over a 5-year period (1956-1960). Tissue specimens originated from dogs examined at the University Veterinary Clinic and patients of veterinary practitioners. The material was somewhat biased toward oral lesions because of special interest on the part of one of the staff.

After histopathologic study, the neoplasms were classified into 14 (51.8%) benign and 13 (48.2%) malignant melanomas. Benign lesions were subdivided: 3 (11.1%) of the compound type, 9 (33.3%) of the dermal type and 2 (7.4%) undetermined (ulcerated lesions, impossible to say if junctional activity present).

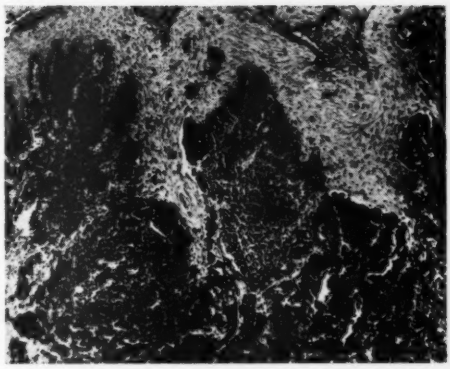


Fig. 16. Canine cutaneous malignant melanoma (foot)—marked junctional activity with theques. Note presence of pseudo-epitheliomatous hyperplasia; x175.

Significant Clinical Data: A. *Benign Melanomas* (14)—1. *Mean age*—7.9 years for dermal type, 3.5 for compound; 2. *Site*—head in 71.4% of dermal type (28.6% eyelids), none of dermal lesions located on acral extremities or in oral cavity; and 3. *Configuration*—almost all tumors raised or pedunculated.

B. *Malignant Melanomas* (13)—1. *Mean age*—9.5 years; 2. *Sex* (12)—66.7% male; 3. *Site* (12)—oral cavity in 75%, digits or foot in 25%; 4. *Description*—tumors tended to be darkly pigmented and infiltrated, 1/3 had regional lymphadenopathy.

Significant Histopathologic Data: 1. The 3 tumors of the compound type (2 on back, one on gingiva) showed the same degree of junctional activity as those in the initial series of the text. 2. All malignant melanomas showed junctional activity. Four (31%) demonstrated extensive epidermal theques. Three of these arose from the oral cavity and one from the foot (all sites where rete ridges may be present normally). The last mentioned is the first extra-oral malignant melanoma that we have seen with marked junctional change (Fig. 16).

COMMENT

1. Benign melanomas tended to occur in younger animals than did malignant lesions.

2. Additional evidence was presented that the degree of change in melanomas may be related to the presence or absence of rete ridges in the normal anatomy of the part.

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Small Animal Clinic

Embryonal Gland Transplantation Studies

These cases are presented to stimulate the interest of veterinarians in the use of embryonal gland implantation as a possible correction of some related conditions.

Case No. 1: A silver Collie puppy, one of those unusual colored dogs which apparently results from combining of 2 genetic factors which alone are harmless but when homozygous, act lethally, was faring badly. When given cortisone, it responded as though the condition was the result of an adrenal insufficiency.

Following the excellent results reported by Dr. H.S.N. Greene in curing Addison's disease by transplantation of embryonal adrenal glands in human beings, the silver Collie was treated similarly. The adrenal glands of a near full term Beagle fetus were placed in a sterilized stilbestrol implanter, such as was used in placing pellets in poultry. This was pushed into an anesthetized area of the 4-month-old puppy's thigh, the plunger pressed and the implanter withdrawn.

The pup was given cortisone for 3 weeks following gland implantation and then medication was withdrawn. From then on the owner reported that the dog acted and grew normally.

After it was grown, the dog developed what the attending veterinarian diagnosed as pneumonia. The dog died but the owner wisely had it necropsied with especial reference to the implant. The veterinarians at Brookhaven Laboratories on Long Island reported that the gland had grown to normal size and that death had been caused by pneumonia.

Case No. 2: A 5-year old Redbone bitch developed a condition diagnosed as diabetes insipidus. She lost weight, developed an almost insatiable thirst (she drank 3 gallons of water one day) and a huge appetite, and became so restless she had made a trench in the sand of her run from ranting back and forth. Her first 2 heat periods had been normal and she produced 2 excellent litters of puppies but the next 3 were abnormally short. The first lasted only a few days but she mated and produced 4 puppies. The next 2 were not over 6 days long, and she would not copulate. Urine tests were characteristic of diabetes insipidus.

She continued to lose weight even on a high fat diet so an embryonal pituitary transplant was tried. A Beagle fetus 50 days old was used. The pituitary was so small that it was impossible to dissect it out without other tissue. This was implanted deeply in the thigh muscle of the bitch.

Whether the transplant corrected this condition it cannot be certain. Two and one-half months later she began to slow in her activity; her food and water consumption became less.

By 3½ months she was apparently normal. The specific gravity of her urine was now in the normal range. She came in heat and had a normal length period, was bred and whelped 12 puppies. For 3 years she produced a litter every 6 months.

The symptoms began to slowly return by the time the bitch was 8 years old. She began to lose weight, developed polydipsia

again and became very restless, so she was destroyed. It was concluded that the transplanted tissue was no longer functional if indeed it was the transplant which had corrected the condition for 3 years.

No claim is made that either transplant had alleviated the symptoms of the ailments which these dogs manifested. Many more transplants will have to be made before the possibility of neither or both being coincidences can be ruled out. However, careful tests were made on both dogs to determine the presence of parasites. Both were maintained in kennels with other dogs, none of which exhibited these ailments.

It will be interesting to see what results more of the same kinds of transplants by other veterinarians will yield.

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A high-speed, air-bearing, air turbine dental handpiece is shown disassembled. Turning at 260,000 r.p.m. the unit is incorporated in a dental handpiece and built by The Garrett Corporation's AiResearch Manufacturing Division, Phoenix, Ariz. Official U. S. Air Force Photo.

Summer Care of Dogs

With summer weather here, your clients have been reminded by the Ken-L-Ration Nutritional Research Kennels in Barrington, Ill. that these are the days when dogs are most uncomfortable, restless and tend to roam more than usual.

Many owners clip their dog's hair to ease the discomfort from heat. A dog's trim should not be cropped too close, because canines sunburn as easily as humans do, and overexposure to the sun can create nasty and painful blisters upon a dog's skin. Unless the owner is highly skilled in clipping, the job should be done by a professional.

Long-haired dogs, such as Collies, should be brushed often in late spring and early summer to remove the sheddings of their fine winter coat which lies beneath their shaggy outer covering. If this shedded hair is not removed, it may mat down and serve as a collection station for dirt, grime and moisture, thus causing a great deal of discomfort to the dog. However, a well-cared-for, long-haired dog is probably more comfortable than most humans on days when the temperature soars. His coat serves as insulation against heat, and his tongue and foot pads exude perspiration.

If a dog is penned in the open, he should have access to shade and water at all times. A raised platform should be provided upon which he can rest. Dog owners should not be alarmed if their dogs do not eat as much during hot weather. Most dogs will eat only as much as their systems can take. Owners should offer their dogs normal amounts of food but in smaller portions and at more frequent intervals.

Dogs not kept in fenced-in areas should never be exercised immediately after a meal during hot weather. In fact, they should be given major exercise in the morning or late at night, with only brief walks in daylight.

Owners whose dogs accompany them in cars should make sure that there is adequate ventilation at all times. When the car is parked, enough shade should be present to prevent virtual baking of the occupant. Chances are that on very hot days the dog would prefer to remain at home in some cool confine such as a basement.

Guest Editorial

The Versatile Veterinarian

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The ramifications and potentialities of veterinary medicine are so extensive that even members of the profession are not fully conscious of the broad scope. This review serves as a refresher to the busy veterinarian and provides excellent background information for counsel of young men who might be interested in a career as veterinarian.

In 1956, Mr. Charles E. Wilson, then Secretary of Defense, shook the veterinary profession down to its toes with his order designed to virtually abolish the Army Veterinary Corps. The Corps was established by an act of Congress in 1916, and had been considered an essential part of Army medical services ever since. Elimination of the Corps would have been a serious blow to the veterinary profession. But equally serious was the order's apparent reflection of a belief that as the horse vanishes from the American scene, so should the veterinarian. Is this a common conception? If the veterinary profession is not like the old soldier just fading away, what is its role in today's society?

There are presently over 20,000 veterinarians in the United States, and the number is increasing by about 700 each year. Approximately one-half are in general clinical practice, and horses are in relatively short supply these days. The U. S. Department of Agriculture reported that the number of horses and mules on farms and ranches decreased from something over a 6 million average for the 10-year period 1948-1957, to just over 3 million in 1959.

Though these 3 million horses have the highest dollar value of any time in the history of the United States, they will not support approximately 10,000 practitioners. But there has been a corresponding increase in numbers and value of other domestic animals in the United States along with the drastic decrease in horse numbers. The health and economical production of these animals requires the services of many practitioners. It is estimated that there are over 90 million head of cattle, including 30 million dairy cows; 57 million hogs; 32 million sheep; and 300 million mature chickens. Almost 2 billion broilers and 100 million turkeys will be produced in 1961.

The modern veterinary practitioner is as far removed from the livery stable and the crude nostrums of old as the present-day physician is from barber shop surgery and the leech. He uses the newest biological agents, drugs and surgical technics, often before they are adopted or modified for use on man. He uses the latest methods of diagnosis, vaccination, sanitation and quarantine. He recommends and supervises the use of hormones and medicated feeds. He uses new technics, such as artificial insemination, to aid in the development and more economical production of better livestock and poultry. The large animal practitioner may have a 2-way radio system between car and office to permit prompt response to emergency calls and more efficient utilization of time.

In the midst of all this scientific progress, of course there is still an occasional call to treat such home-diagnosed ills as "hollow-horn," "wolf-in-the-tail," and "moon-eyes." The better part of wisdom often decrees no argument over diagnosis, so long as professional treatment is accepted.

The large animal practitioner makes an important contribution to the nutritional standards of the consuming public, as well as to the economic welfare of his clients. Each of us in the United States consumes an average of almost 1,500 lb. of food each year, a total of over 250 billion lb. About 110 billion lb. of this total, or 650 lb. per person, are dairy products, eggs, meat, fish and poultry, all foods of animal origin. It is easy to understand that continuing advances in veterinary science and in the quality of veterinary services will be essential to maintenance of this supply of protein foods in years to come. The Census Bureau estimates that our population will increase to over 200 million by 1970, and will be in the range of 231 to 272 million by 1980.

A study in 1955 by the American Veterinary Medical Association indicated that for every dollar a livestock owner spent for veterinary service, he received $5.78 return on his investment. Based on this rate of return, an economist of the U. S. Department of Agriculture estimated that in 1955, the farmers in the New England and New York area alone received $80,000,000 of their income as a result of veterinary medical service. Moreover, this made no allowance for previous years of veterinary advice and preventive programs that have resulted in healthier, more productive livestock.

In addition to their other activities, many veterinary practitioners serve as advisors to rural families, local physicians and health agencies on diseases of animals transmissible to man. Many also engage part time in official animal disease testing programs, vaccination programs and food inspection activities which contribute toward the protection of human health and welfare. They are the source of animal morbidity and mortality data, essential for the planning and conduct of preventive and control measures by health and agricultural agencies.

Specialized Practices

Approximately 25% of all veterinarians in this country engage in specialized practices. Some specialize in dairy practice, others in poultry, and a few in horses.

At race tracks and fairs veterinarians also provide interesting and essential services. As an example, each year in Missouri,

county, district and state fairs utilize the services of over 300 veterinarians to carry out the required tests and health examinations of the animals to be exhibited. They collect samples of saliva from winning horses to test for stimulants and give special assistance to the F. F. A. and 4-H Club girls and boys.

Veterinarians are on the staffs of over 30 zoos throughout the country, and are the directors of at least 3 of the largest (the Cleveland Zoo, the Griffith Park Zoo at Los Angeles, and the National Zoological Park, Washington, D. C.). Reports by the latter show that during each year approximately 4 million persons from all over the world visit there to view the 2,300 animals on display. Though few in number, these zoo veterinarians make a unique contribution by protecting the health of both rare and common animals on public display.

More than 87% of specialized veterinary practices, however, are pet or small animal practices. The small animal practitioner is a very important asset to the modern community. He contributes to the enjoyment and emotional well-being of pet owners at the same time that he ministers to the health needs of the pet population.

There are now in the United States about 26 million dogs owned by 18 million families. Moreover, it is estimated that there are at least 27 million cats, 23 million birds, 175 million fish, 3½ million turtles, 125,000 monkeys, and 15,000 skunks kept as pets. These pets all play an important role in the lives of their owners, some over and above the mere companionship afforded. Many are entered in competitive shows each year; about 2,500 dogs are entered in the annual Westminister Kennel Club Dog Show at Madison Square Garden, alone. Watch dogs and hunting dogs are numerous. Very significant, of course, are the seeing-eye dogs and others used as protective companions.

The veterinary profession is deeply aware of its responsibilities in this area. It works closely with humane societies, animal protective leagues and related organizations. Most important, it strives to provide the finest animal medical care possible. The 2,500 modern small animal clinics in the United States compare favorably with human medical clinics in the facilities and professional services offered.

The American Animal Hospital Association, founded in 1933, has as its aim the maintenance of high standards for professional service and hospital facilities in the care and treatment of dogs, cats and other pet animals. The Association gives annual awards to senior veterinary students who write the best essays on ethics, thus impressing on future practitioners their professional responsibilities to the pet owners of America.

Regulatory Veterinarians

A very important number of veterinarians are engaged in a never-ending attack on diseases which might otherwise devastate our livestock population. The work of these veterinarians in departments of agriculture is generally known, but may not be fully appreciated. There are about 1,500 veterinarians working in the U. S. Department of Agriculture. There is a state veterinarian in each state, and numerous others on the staffs of state agricultural agencies. Some carry out research on animal diseases, parasitology, toxicology and nutrition. Others conduct or cooperate in livestock and poultry disease control programs. For example, the U. S. Department of Agriculture estimates that losses from brucellosis in cattle have been reduced from about $92,000,000 in 1947 to below $25,000,000 annually at present. Of 15 million cattle carcasses slaughtered under Federal inspection in 1953, 457 were condemned for tuberculosis; in the fiscal year of 1960, only 188 of 18,454,319 were condemned for this reason.

Current field activities of the U. S. Department of Agriculture and state agencies include programs to eradicate these costly diseases and others, such as anaplasmosis; scabies in cattle, sheep, and goats;

hog cholera and erysipelas; and fowl paralysis, pullorum disease and Newcastle disease in poultry. These agencies are called on to control outbreaks of diseases such as vesicular exanthema and anthrax, which may threaten livestock production or economy.

These disease control programs in our modern day society are just as important as they were in the past. During 1952-53, vesicular exanthema of swine spread from a confined area in California to 42 states, and caused major disruption of domestic and foreign marketing before it could be controlled. An anthrax outbreak during the late summer of 1957 in Oklahoma and Kansas killed an estimated 1,503 cattle, 15 horses and mules, 39 sheep, 68 hogs, and 2 other animals on 741 premises. The movement and marketing of livestock and milk were put under severe restrictions, causing serious loss. To control the outbreak, 203,-140 animals were vaccinated.

Another job of USDA veterinarians is to prevent the introduction of devastating animal diseases from foreign countries into the United States and to eradicate them if they do gain a foothold. More than 25,000 animals, ranging from ordinary mules to rare jungle animals like the okapi, are examined each year at air and ocean ports of the United States by veterinary inspectors. Nearly all the poultry and more than ½ of the livestock coming from overseas travel by air, making possible the arrival of animals which appear to be healthy but which are in the incubation stage of disease.

The U. S. Department of Agriculture has built a new laboratory on Plum Island, New York, for research on foot and mouth disease and other virus diseases. A large laboratory has recently been completed at Ames, Iowa for other research on animal diseases and parasites. In addition to the constant threat of foreign animal diseases, there is ample evidence of need for these laboratories and for continuing programs of disease eradication. Even though the United States is reputed to have one of the healthiest livestock economies in the world, American livestock producers suffer losses of over 2½ billion dollars annually from animal disease agents and parasites. Mastitis alone exacts a yearly toll of ¼ billion dollars from dairy farmers. Poultry disease losses reach an estimated $240,000,000 annually.

Quarantine and eradication programs are expensive. When foot-and-mouth disease broke out in Mexico in 1947, the United States cooperated with the Mexican Government in a 5-year fight which resulted in 1 million animals slaughtered, and 60 million doses of vaccine used; but the cost of eradication is infinitesimal when measured against the economic losses and the human deprivation and misery which result from "living with" these animal scourges.

When the meat inspection services of the U. S. Department of Agriculture were initiated in 1906, inspection was provided in 163 establishments located in 58 cities. On June 30, 1960, inspections were being conducted in 1,396 establishments in 572 cities and towns. Veterinarians in the Meat Inspection Division supervise and conduct the inspection for wholesomeness of all livestock slaughtered in those plants which engage in interstate commerce. During the year July 1, 1959, to June 30, 1960, they inspected over 107 million animals before and again after slaughter. Meat and meat food products prepared and processed under supervision totaled 18,698,087,787 lb.

The 7 chemical control laboratories and the biological control laboratory of the division examined more than 70,000 samples and specimens. Almost 490 million lb. of meat and meat food products were examined for compliance with specifications or condition for other government agencies. Over 872 million lb. were examined for entry from foreign countries.

About 3 billion dollars are spent at retail each year for poultry. The Poultry Inspection Branch of USDA is putting into full effect a new law which requires inspection of all poultry processed by plants shipping products across state lines. An inspection service has been provided on

voluntary application and compliance with sanitation requirements by poultry processors for the last 29 years. In 1959, under a gradual integration of the old voluntary and the new mandatory programs, 4¾ billion lb. of ready-to-cook poultry were certified as wholesome from a total 1,607,000,000 head of chickens, turkeys and ducks inspected.

Veterinarians in these inspection programs are in a position to observe the presence of livestock and poultry diseases, and alert animal disease control officials to special problems so that they may move in quickly and efficiently. The primary mission of these programs is to assure the consuming public of clean, wholesome, unadulterated and truthfully labeled meat. In 1959, poultry carcasses weighing 95 million lb. were condemned by the Poultry Inspection Branch as unfit for human consumption. Of the large animals inspected in fiscal year 1960 by the Meat Inspection Division, over 255 thousand were condemned. Several million livers and other parts of carcasses were also found unfit. Over 34 million lb. of meat and meat food products were condemned on reinspection and destroyed. In addition, 1,846,898 lb. of foreign meat and meat products were either refused entry or condemned.

Each person in the United States consumes about 190 lb. of beef, veal, lamb, pork and poultry per year. Federal inspection of about ¾ of the 32 billion lb. total costs less than a penny per pound, or only about 18 cents per person. This is a small cost indeed! But, to more adequately staff these Federal services, many more veterinarians are needed.

A further activity of USDA veterinarians is to supervise the production of 2½ to 3 million doses of veterinary serums, vaccines, bacterins and diagnostic agents to assure the efficacy and safety of the products.

As might be expected, veterinarians in industry play a major role in research, development and production of biologics and various drugs and antibiotics, particularly those used for veterinary purposes. According to an estimate by an industry official, antibiotic sales for veterinary use in 1958 totaled 65 million dollars at the manufacturers level, 30 million dollars in animal feed supplements and 35 million dollars in veterinary drug products.

Before being marketed, all new antibiotics and drugs which come within the statutory definition of a "new drug" must be cleared by the U. S. Food and Drug Administration as safe for the intended use. Veterinarians in industry may run acute, subacute and chronic toxicity tests on animals to determine the safety of newly developed pharmaceutical compounds. The Veterinary Medical Division of the FDA Bureau of Medicine checks the validity of data submitted by industry on new drugs intended for veterinary use; and, if deemed necessary, may conduct clinical tests of a product before clearing it.

Medical Interchange

The veterinary profession has made notable contributions to the broad field of medicine and human health. The work of veterinary practitioners and the importance of foods of animal origin have been mentioned. More specific contributions are numerous, but their origin may be unknown to the average person today.

Field investigations by Dr. Cooper Curtice of the Bureau of Animal Industry led to the discovery by Smith and Kilbourne in 1893 that Texas fever of cattle was caused by a protozoan parasite, carried and transmitted by a particular species of tick. This research is reported to have cost $65,000, and returned to the livestock producer a saving of 60 million dollars annually. Far more important was the fact that it opened the field to discovery of the role of insects as vectors of many human, as well as animal, diseases such as mosquito-borne malaria and yellow fever and tick-borne typhus.

Dr. Maurice Hall and his co-workers in BAI discovered that carbon tetrachloride (a common cleaning fluid) was an effective treatment for hookworms. This led to

the development of the improved and safer tetrachlorethylene, used to control this scourge in man.

Dr. Karl Meyer of the Hooper Foundation for Medical Research, San Francisco, is internationally known for his research on bubonic plague, psittacosis, encephalomyelitis and leptospirosis. His classic work on botulism has resulted in virtual elimination of this deadly hazard from both commercial and home canned foods and made possible the modern food canning industry.

Contributions such as the work of Franz Benesch on caudal anesthesia; William Jenner, cowpox and smallpox; Gaston Ramon, tetanus and diphtheria toxoids; Camille Guerin and the B.C.G. vaccine for prevention of tuberculosis; Otto Stader and the Stader splint. The more recent work of Harry Gorman on the prosthetic hip and of Frank Schofield and his discovery of an anticoagulant factor in sweet clover, which led to the development of dicumarol are other milestones stemming from veterinary medicine which have helped to save the lives of millions of people and relieve much human suffering.

But the important thing is the renewed recognition since World War II of the basic oneness of all medicine, human and animal. This has resulted in steadily increasing participation by veterinarians in official federal, state, and local health programs.

These veterinarians engage in a variety of activities. They conduct or advise on food inspection and sanitation services, particularly state and local meat and milk hygiene programs. These and related animal disease control programs have aided in reducing the incidence of scarlet fever, diphtheria, typhoid, streptococcal sore throat, brucellosis, bovine tuberculosis, tapeworms, tularemia, salmonellosis and anthrax.

A major role of the veterinarians in public health agencies is in research, development of diagnostic and laboratory methods, special training and advisory services, and epidemiological investigations and preventive medicine programs concerned with the zoonoses. Over 100 zoonoses have been recognized to date. More than 20 are of considerable significance in the United States. Prevention of these diseases in man depends to a large extent on eradication or control in animals.

Rabies is an example. There are approximately 60,000 people exposed to rabies annually in the United States. Fortunately, an average of only about 22 persons have died annually during the last 20 years as a result of contracting this disease (there were 7 deaths in 1959). Over ½ of these, however, were children under 15 years of age. Moreover, the knowledge that the disease, once contracted, is fatal causes severe anxiety and fear in more than ½ million people bitten by animals each year. The widespread presence of rabies among wild animals such as foxes, skunks and bats serves as a reservoir of infection and makes vaccination of dogs and other pets and other official control measures even more essential than might otherwise be the case.

The real incidence and significance of many of the zoonoses is just being discovered. Leptospirosis, spread through the urine of affected animals, is an example. In animals this is an acute generalized infection, often causing abortion. It is common among cattle, swine, dogs and rodents, and wild animals are frequently infected with many different types. Leptospirosis has replaced brucellosis as a major economic disease of domestic animals in the United States. In man it is an acute systemic infection with meningeal signs in severe cases. Jaundice, renal insufficiency and hemolytic anemia appear in terminal cases. Fever, chills, headache, muscular pains, fatigue and malaise are common symptoms.

The investigation, surveillance and resolution of problems associated with the zoonoses generally require the cumulative efforts of a number of persons of varied professional training and experience. In addition to his own particular activities, the public health veterinarian usually serves as a liaison representative on the zoonoses between the health agency and

representatives of other governmental agencies, industry, educational institutions and professional organizations.

In 1959, a research center for zoonoses in the United States was established at the University of Illinois. Under the direction of Dr. Carl Brandly, dean of the College of Veterinary Medicine, it provides for studies in comparative medicine by veterinarians, physicians and other scientists.

The United Nations World Health Organization (WHO) has recognized the zoonoses as a major world concern because they constitute an important cause of sickness and poverty brought about by acute and chronic infections in human beings. They cause extremely large economic losses to agriculture and trade. Several expert committees of WHO have prepared monographs and technical reports on food hygiene, the zoonoses and veterinary public health practice. The Pan American Zoonoses Center, Azul, Argentina, was established in 1956 to provide services related to zoonoses control and eradication campaigns for health departments, agricultural agencies and educational institutions of the Americas. The center offers training, consultation, field demonstrations, confirmatory diagnostic tests and research services on diseases such as rabies, brucellosis, hydatidosis, viral encephalitides, leptospirosis, trichinosis, psittacosis and anthrax.

Leading veterinarians from the United States participate in the work of WHO and serve on medical research, advisory and study teams sent to foreign countries.

Military Veterinarians

How does the veterinarian fit into this modern age of geometrically-multiplying scientific and biological discoveries? Has his profession, which was once literally geared to the "horse age," been able to adapt and apply itself to the dynamically changing social and technical world of today? For example, what about military veterinarians, the subject of the startling order handed down by Secretary Wilson in 1956? Was Mr. Wilson justified in assuming that machines had ended the need for veterinary services in the Department of Defense?

Veterinarians were first utilized by the military forces because of disasters resulting from immobilization of armies when transport animals were sick and disabled. However, the only horses in the U. S. military forces today are a few kept at Fort Myers, Va., for ceremonial purposes. It is evident that the duties of the modern military veterinarian must bear little resemblance to those of early days.

There are about 775 veterinary officers in the Army and the Air Force, supervising approximately 2,500 highly trained enlisted personnel. These veterinarians act as consultants and advisors to military physicians on health matters related to all aspects of food hygiene. They advise on and supervise food inspection activities, quality standards, storage, transportation and sanitation factors in the preparation and service of foods. They participate in research on food safety, processing methods, development of special combat rations and other problems, such as in-flight feeding, radiation preservation of foods and intentional or accidental chemical, microbiological or radiological contamination of food sources or supplies.

During a recent one-year period, food under military veterinary inspections totaled over 4 billion lb.; and during a similar period, over 61,000 food source establishments were inspected. The food inspected by military veterinarians for central procurement purposes in 1958 was valued at approximately 250 million dollars.

Other areas of military veterinary activity involve implementing and supervising animal disease control programs, quarantines and related measures concerned with protecting the military community against zoonotic diseases. Military veterinarians also assist medical officers on the sanitary and medical aspects of housing, eating establishments, recreation facilities, waste disposal and other factors affecting the general sanitation of the military community. Their duties include training some 500 sentry dogs

annually and supervising about 2,500 on hand, producing and managing research animals and participating in research on surgery, physiology, human stress, deceleration, shock, burns, pathology, virology, space medicine, radiobiology, epidemiology and related aviation and military medical problems.

Their work extends to many areas outside of the United States. It produces incidental benefits for civilian populations here and abroad through improved food products, safer food supplies and improved preventive medicine and sanitation practices in communities adjacent to military installations.

What of Mr. Wilson's order? After thorough study, it was set aside in 1958 by Secretary of Defense Neill H. McElroy, and the Veterinary Corps was given new research responsibilities, in addition to authority for continuation of previous services.

Of course, participation by veterinarians in new areas of research is not limited to those in the Armed Forces. The knowledge of a disease or pathologic process is made more complete when it is known or studied in both man and lower animals. Such comprehensive studies may involve physiology, pathology, bacteriology, virology, mycology, parasitology, immunology, genetics, ophthalmology, dermatology and the chronic, deteriorative or nutritional illnesses. Epidemiological principles, pharmacology, laboratory disciplines and surgical technics may be important. Veterinarians throughout governmental agencies, industry and educational institutions are active in basic and applied research, significant to both human and veterinary medicine.

In addition to supervising, carrying out or cooperating in research on such problems, veterinarians direct the selection, breeding, nutrition and professional care, including disease prevention and control, of all types of laboratory animals. For certain highly critical studies, colonies of "germ-free" and "specific pathogen-free" animals are maintained. Laboratories in drug companies and other institutions use 20 million mice and 200,000 monkeys a year. Other animals used in research include dogs, guinea pigs, rats, hamsters, rabbits, wild birds, domestic poultry and even toads. Veterinarians operate experimental surgery suites for large medical research organizations, including the preoperative preparation of animal subjects and their postoperative care.

Veterinary Education

The training received by veterinary students depends upon the adequacy of the staffs in the veterinary colleges. These staffs must maintain an extremely high level of excellence to warrant accreditation of the colleges by the Council on Education of the American Veterinary Medical Association. Many important advances in medical science have come from the veterinary research of our various educational institutions. Actual clinical practice under skilled supervision and association with research projects under way give veterinary students an understanding of the broad scope and potentialities of the profession.

The education received by veterinarians is quite comparable to that of physicians and dentists. The 4-year professional curriculum covers the broad scope of medicine: anatomy, including histology and embryology; physiology and biochemistry; pathology, microbiology and immunology; parasitology; pharmacology and materia medica; food hygiene; diseases of the reproductive system; medicine and surgery; and large and small animal clinics. Not less than 4,000 hours of classroom, laboratory and clinical instruction are required.

At present there are 17 colleges of veterinary medicine in the United States and 2 in Canada which are accredited by the Council on Education of the American Veterinary Medical Association. All require at least 2 years of preprofessional college study, which usually includes chemistry (inorganic, organic and biochemistry), zoology, botany and physics.

Actually, most of the students entering the 4-year veterinary course have more than

the required 2 years of professional college training. In the years 1949 and 1950, 27% had 3 years, and an additional 26% had 4 years or more. In 1951, 32% had 3 years, and another 28% had 4 years or more.

In 1956, of 942 freshman veterinary students enrolled, 207 had earned bachelor degrees and 11 had Master of Science degrees. In 1957, 231 of 1,037 freshman had B.S., and 11 had M.S. degrees (55% had 3 or more years of professional training). In 1958, 25.8% had 3, an additional 21.2% had 4, and another 9% had 5 or more years of college work to their credit (15 had master degrees, 234 had bachelor degrees and one had a Ph.D. degree). Of the 1,058 first-year veterinary students in 1959, 54% had 3 or more years of professional training; 286 had bachelor degrees; 28 had master degrees; and one had a Ph.D. degree.

Before being permitted to practice, all veterinary graduates must pass written and oral examinations given by state veterinary examining boards. Postgraduate training is not neglected. In the United States and Canada veterinarians earned 53 M.S., 18 Ph.D. and 30 public health advanced degrees in 1958, and 86 M.S., 23 Ph.D. and 25 public health advanced degrees in 1959.

The fairer sex is very definitely represented in all this. There are several women in the graduating classes each year. At the 1958 annual meeting of the Women's Veterinary Medical Association, technical papers ranged from "Fertility of Horses" by Dr. M. Phyllis Rose of Berwyn, Pa., to "The Veterinarian in Atomic Research" by Dr. Louise S. Lombard of Lemont, Ill. Dr. Patricia O'Conner, elected president of the Association, is a veterinarian at the Staten Island Zoo.

Wives of veterinarians are also very much in the picture. The Women's Auxiliary to the American Veterinary Medical Association is older than either the medical or dental auxiliaries. Organized in 1917 by 55 wives, it now has 7,500 members. Among other activities, it encourages high scholastic standards through awards to outstanding veterinary students.

Since we are concerned these days with comparisons between the United States and Russia, it is interesting to note the numbers of veterinary schools and personnel in the Soviet Union. According to the December 1957 issue of *Veterinariya* (Moscow), there were 33 veterinary colleges in the Soviet Union in 1956; there were 31,000 veterinarians assisted by 40,000 veterinary technicians, graduates of veterinary technical high schools. Although Russia and her satellite countries are considered by observers to be somewhat behind the United States in some phases of veterinary research and practice, it is significant that they grant high regard and priorities to veterinary medical activities and veterinary education. A member of a U.S. team which visited Russia in 1958 reported that there were then about 42,000 veterinarians and 49,000 assistants in the U.S.S.R. and that approximately 3,500 new veterinarians were being graduated annually from 34 colleges.

The Future

Judging from current activities and needs, the future seems bright indeed. More animals and foods of animal origin for the rapidly expanding population will call for more veterinarians in clinical practice, industry and regulatory agencies. It has been estimated that the services of approximately 1,500 additional veterinarians are needed in state and local health agencies alone. The ever expanding areas of medical research offer almost unlimited opportunities for veterinary participation.

Lord Bryce said, "Medicine is the only profession in the world that labors incessantly to destroy the reason for its existence." That goal is not yet in sight, but in the near future new disease control methods and medical technics may make those of today as outmoded as those of 100 years ago seem to us now. If so, it seems certain that the veterinarian will have made his share of major contributions, just as he has in the past.

Clinical Research

Morphology of Adrenal Capsular Nodules in the Bovine

J. M. Delphia, Ph.D., D. F. Eveleth, Ph.D., D.V.M., R. Montgomery, B.S., and Marjorie C. Paulsen, B.S.
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Accessory adrenal cortical nodules and accessory adrenal glands (cortical nodules with medullary tissue in the center) are known in the rat[4] and in man.[2,3,5] Such accessory cortical nodules or accessory adrenal glands, if functional, might play important endocrine roles in conjunction with the main adrenal glands. The present paper reports the study of the structure of accessory nodules in the capsules of the adrenal glands of the bovine.

Gruenwald[3] discussed the development of adrenal cortical nodules in the capsules of the adrenal glands of man. He agreed with previous workers that such nodules were numerous in infants and decreased in numbers with age of the individual. According to Gruenwald this was brought about by fusion with the adrenal gland. Jaffe[6] reported medullary tissue in accessory cortical nodules in the celiac region in man. Accessory cortical nodules have been observed in the adrenal capsules of the bovine by Smollich[6] and Delphia *et al.*[1]

Clinical Observations

Both adrenal glands were obtained from animals in the A, B, and D series, N-457-2 and N-476 (see Table 1). In the N-481 and N-485 series only 1 adrenal gland was obtained. These animals and N-457-2 were slaughtered at the Armour Packing Company, West Fargo, N. D. Post-mortem examinations were conducted by the Veterinary Science Diagnostic Laboratory staff of North Dakota Agriculture College for animals in the A, B & D series and N-476.

At the time of slaughter or post-mortem examination of the animals, adrenal glands were sliced into several parasagittal sections and fixed in either Bouin's fluid or Lavdowsky's fluid. After fixation the capsules were removed carefully and accessory cortical nodules observed. Nodules not connected to the cortex or the main gland were

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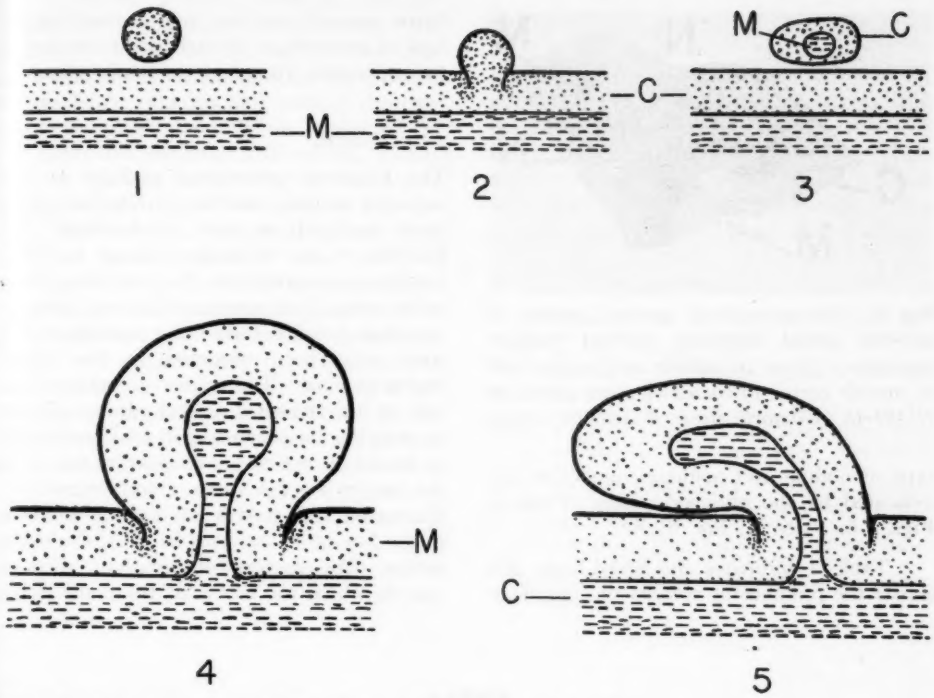

Legend for Plates: C — Cortex, M — Medulla, N — Nodule.
Fig. 1. Illustration of cortical nodule lying in capsule of adrenal gland, as in N-481-13. Fig. 2. Illustration of cortical nodule connected to cortex of adrenal gland, as in N-485-18. Fig. 3. Illustration of nodule containing both corticular and medullary tissue, as in N-481-37. Fig. 4. Illustration of spherical nodule connected to both cortex and medulla of adrenal gland, N-481-37. Fig. 5. Illustration of ovate nodule connected to both cortex and medulla of adrenal gland, N-485-19.

removed and prepared for histological section, taking adequate cortex and medulla of the main gland adjacent to the nodule. All tissues were sectioned at 6 microns by routine histological methods. Hematoxylin and eosin stain was used for routine examination. Gomoris stain was used for minute capsule differentiations.

A total of 127 animals were involved in the present study. Nodules observed in this study ranged in greatest length and width from 0.5 mm. to 12.0 mm. and 0.5 mm to 8.5 mm. respectively. The general shape varied from nearly spherical to broadly ovate. The position for the connection of the cortex of the main gland to cortical tissue of a nodule varied from the base of the spherical nodule to 1 edge (lateral margin) of a nodule (Plate I, Figs. 4, 5). The above statement holds true also for connection of the medulla of the main gland to the medullary tissue in the cortical nodule. Cortical nodules connected to the main gland were connected by union of the glomerular, fasciular and reticular layers of the nodule with the respective layers of the cortex of the main gland (Plate II, Fig. 6).

Four cases were found in which the central portion of the nodule was extremely vascular (N-481-25; N-485-18; N-485-50 and N-485-59). No medullary tissue was observed in these nodules (above). The significance of the extreme vascularity is not known. One or more examples of each

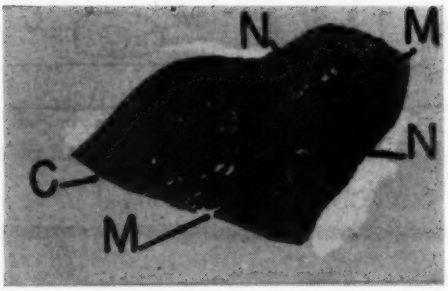

Fig. 6. Photograph of stained section of adrenal gland showing cortical nodule, medullary tissue in nodule and connection of nodule cortex to cortex of main gland, in N-481-48. Gomoris stain, 4 magnifications.

type of nodule and nodular connection are indicated by the attached plates (Plate I, Figs. 1-5; Plate II, Fig. 6).

Table 1 indicates the breed, age, sex status· the presence or absence of medullary tissue in each nodule, and connection or lack of connection of each nodule with the corresponding tissue in the main gland.

Discussion

The existence of cortical nodules in the capsules of the adrenal glands has been cited previously in cattle by Smollich[6] and Delphia *et al.*[1] Medullary tissue in these nodules is recorded for the first time. It is to be noted that accessory adrenal nodules (cortical nodules containing medullary tissue) have been observed in the celiac region in man.[5] The origin of cortical nodules in the capsules of the adrenal glands in man has been considered by Gruenwald[3] as fusion of embryonic cortical masses with the cortex of the main gland. Smollich[6] illustrated the growth of cortical nodules in the bovine as outgrowths from the main cortex. The present observations show 1 case in which the cortex of the main gland

TABLE 1.
Structure of Adrenal Nodules

Animal Number	Age	Sex Status	Breed	Nodule containing corticular tissue only	Corticular and medullary tissue	Nodular cortex to adrenal cortex	Nodular medulla to adrenal medulla
A-9-332	1 mo.	Male	Hereford	X			
B-337	Newborn	Male	Hereford	X			
D-315	6 mo.	Female	Guernsey		X		
N-457-2	30 mo.	Female	Hereford		X	X	X
N-476	Newborn	Female	Shorthorn		X	X	X
N-481-13	30 mo.	Castrate Male	Hereford	X			
N-481-18	18-24 mo.	Castrate Male	Hereford	X			
N-481-25	20 mo.	Castrate Male	Hereford		•		
N-481-28	20 mo.	Castrate Male	Hereford	X			
N-481-31	18 mo.	Castrate Male	Hereford		(1)X	(1)X	(1)X
N-481-32	20 mo.	Castrate Male	Hereford		(2)X X	X	X
N-481-37	20 mo.	Castrate Male	Hereford		(1)X (2)X	(1)X	(1)X
N-481-48	18 mo.	Castrate Male	Hereford	(1)X (2)X			
					(3)X (4)X	(4)X	(4)X
N-481-52	30 mo.	Castrate Male	Hereford		X	X	X
N-485-18	18 mo.	Female	Hereford		•	X	
N-485-19	18 mo.	Female	Hereford		X	X	X
N-485-40	18 mo.	Female	Hereford	X			
N-485-50	18 mo.	Castrate Male	Hereford		•		
N-485-58	30 mo.	Female	Hereford		X	X	
N-485-59	30 mo.	Female	Hereford		•		

•Nodule contains corticular tissue; center highly vascular but void of medullary tissue.

was connected to the cortex of a nodule containing medullary tissue, while the medullary tissue of the nodule was not connected to its counterpart in the adrenal gland. Eight nodules had neither the corticular nor medullary tissue connected to the respective layers of the adrenal gland; while 8 nodules with both the corticular and medullary region were connected to the respective regions of the main gland. Ten capsular cortical nodules were void of medullary tissue; 4 of these presented possible tissue transition intermediate between non-medullary and medullary condition. These facts suggest that (1) either cortex and medulla or cortex alone is budded off from the main gland and established in the adrenal capsule as accessory adrenal gland or accessory cortical nodule; or that (2) the cortical and medullary tissue in each nodule originate in the capsule and by growth become associated with and connected to the respective portions of the main gland.

Summary

The existence of medullary tissue in cortical nodules in the capsules of the adrenal gland in the bovine is established. The connection of the cortical layers of the nodule to respective layers of the adrenal cortex and the medulla of the nodule to the medulla of the adrenal gland was observed.

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Parakeet the Vector In Salmonella Infection Case

A case of *Salmonella typhimurium* infection in an infant, the first recorded case of human salmonella infection in which a parakeet was the vector, has been reported in New York City.

Drs. Donald Kaye, Henry R. Shinefield and Edward M. Hook from the departments of Medicine and Pediatrics, New York Hospital—Cornell Medical Center, presented a report of a 7-month-old boy who is presumed to have become infected from the droppings of an infected parakeet.

The parakeet could have acquired its infection in the original aviary, in the wholesale concern, in the variety store where it was purchased or even in the home. The patient lived with his parents on the 12th floor of a recently constructed building. There had been no reports of mice or rats in the apartment house. The only animals in the apartment were 2 parakeets. Although both birds were active and apparently healthy, *Sal. typhimurium* was isolated from one of the birds from September 19 to October 8. The birds were not handled by members of the household and were not permitted to fly about the apartment.

They were kept in a cage suspended 5 feet from the floor and feathers and droppings occasionally fell to the floor in an area where the infant crawled and played.

The incidence of salmonellosis among parakeets is unknown. Meyer (personal communication) did not isolate salmonellae from over 25,000 parakeets raised in California and Eastern aviaries from 1932 to 1939. However, he later demonstrated by autopsy culture that 37% of parakeets from a single dealer were infected with *Sal. typhimurium*, and that infection was acquired by association with large South American psittacine birds.

New Eng. Jour. Med., 264:868-869 (April 27) 1961

Medical Interchange

Notes and abstracts screened from the medical literature for their special interest to veterinarians by Lynn Stratton Morris.

Distemper-Measles Immunity Studied

The viruses of human measles and canine distemper are antigenically related, according to studies in dogs reported by James H. Gillespie and David T. Karzon of the Veterinary Virus Research Institute, Cornell University, Ithaca.

Neutralizing and complement-fixing antibodies to measles developed readily in dogs inoculated with live measles virus. The dogs showed no signs of illness and did not spread the infection to unit contact litter mates. Following measles inoculation, 7 out of 11 dogs developed low titers of canine distemper neutralizing antibody. All measles inoculated dogs, including those with no demonstrable canine distemper neutralizing antibodies, were protected against intravenous or intracerebral challenge with virulent Snyder Hill canine distemper virus (at 24-28 and 84 days). The contact controls, not receiving measles virus, became ill and 3 died. The dogs which received distemper virus alone developed distemper neutralizing antibody, but no measles neutralizing antibody although they were maintained in the same isolation unit as their litter mates inoculated with measles virus.

Following inoculation with measles virus and subsequent intracerebral challenge with distemper virus, one dog had no illness and no increase in titer, suggesting that sufficient protection was present at time of intracerebral inoculation to interfere with production of illness and antibody increase.

Dogs used in these studies came from a purebred colony of Beagles, reared and maintained in isolation at the institute. The 19 dogs represented 6 different litters, ranging in age from 5 to 24 weeks at time of measles injection.

Proc. Soc. Exp. Biol. Med., 105:547-551 December, 1960

Puppies Need Human Contact Before 14 Weeks

A puppy must be handled before it is 14 weeks old or it will never wag its tail at the sight of a human being, scientists working at the Roscoe B. Jackson Memorial Laboratory in Bar Harbor, Maine, have found.

If puppies are left alone too long, they become afraid and unwilling to socialize with or take commands from human beings.

Dr. Daniel J. Freedman, now of the Langley Porter Neuropsychiatric Institute in San Francisco, Dr. Orville Elliot, now at Harvard University, Cambridge, Mass., and Dr. John A. King reported their findings in *Science*, 133:1016, 1961. They tested

(Cont'd on page 23a)

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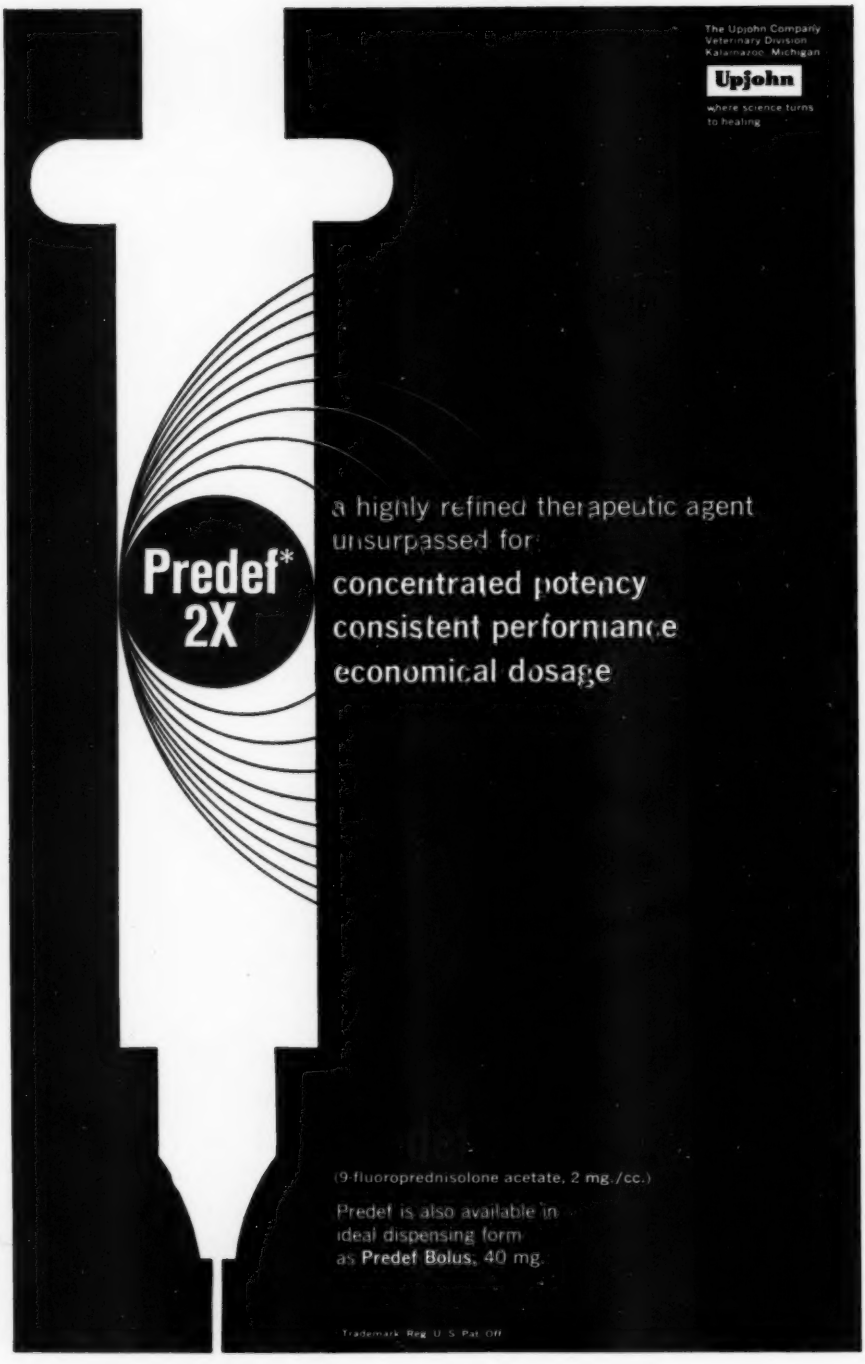
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